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FILE 'MEDLINE' ENTERED AT 14:05:25 ON 12 MAY 2004

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=> s folicle injection
L1            0 FOLICLE INJECTION

=> s lymph node
L2       354385 LYMPH NODE

=> s l2 and injection
L3        20700 L2 AND INJECTION

=> s l3 and CTL response
L4          192 L3 AND CTL RESPONSE

=> s l4 and directly
L5           11 L4 AND DIRECTLY

=> dup remove l5
PROCESSING COMPLETED FOR L5
L6             3 DUP REMOVE L5 (8 DUPLICATES REMOVED)

=> d l6 1-3 cbib abs
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L6 ANSWER 1 OF 3 MEDLINE on STN DUPLICATE 1

2001653914. PubMed ID: 11689645. Epidermal powder immunization induces both cytotoxic T-lymphocyte and antibody responses to protein antigens of influenza and hepatitis B viruses. Chen D; Weis K F; Chu Q; Erickson C; Endres R; Lively C R; Osorio J; Payne L G. (PowderJect Vaccines, Inc., Madison, Wisconsin 53711, USA.. dexiang_chen@powderject.com) . Journal of virology, (2001 Dec) 75 (23) 11630-40. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB Cytotoxic T lymphocytes (CTL) play a vital role in host defense against viral and intracellular bacterial infections. However, nonreplicating vaccines administered by intramuscular **injection** using a syringe and needle elicit predominantly humoral responses and not **CTL responses.** Here we report that epidermal powder immunization (EPI), a technology that delivers antigens on 1.5- to 2.5-microm gold particles to the epidermis using a needle-free powder delivery system, elicits **CTL responses** to nonreplicating antigens. Following EPI, a majority of the antigen-coated gold particles were found in the viable epidermis in the histological sections of the target skin. Further studies using transmission electron microscopy revealed the intracellular localization of the gold particles. Many Langerhans cells (LCs) at the vaccination site contained antigen-coated particles, as revealed by two-color immunofluorescence microscopy, and these cells were found in the draining **lymph nodes** 20 h later. Immune responses to several viral protein antigens after EPI were studied in mice. EPI with hepatitis B surface antigen (HBsAg) and a synthetic peptide of influenza virus nucleoprotein (NP peptide) elicited antigen-specific **CTL responses** as well as antibody

responses. In an in vitro cell depletion experiment, we demonstrated that the CTL activity against HBsAg elicited by EPI was attributed to CD8(+), not CD4(+), T cells. As controls, needle **injections** of HBsAg or the NP peptide into deeper tissues elicited solely antibody, not **CTL, responses.** We further demonstrated that EPI with inactivated A/Aichi/68 (H3N2) or A/Sydney/97 (H3N2) influenza virus elicited complete protection against a mouse-adapted A/Aichi/68 virus. In summary, EPI **directly** delivers protein antigens to the cytosol of the LCs in the skin and elicits both cellular and antibody responses.

L6 ANSWER 2 OF 3 MEDLINE on STN DUPLICATE 2

2001555951. PubMed ID: 11602701. Simian virus 40 large-T-antigen-specific rejection of mKSA tumor cells in BALB/c mice is critically dependent on both strictly tumor-associated, tumor-specific CD8(+) cytotoxic T lymphocytes and CD4(+) T helper cells. Utermohlen O; Schulze-Garg C; Warnecke G; Gugel R; Lohler J; Deppert W. (Heinrich-Pette-Institut fur Experimentelle Virologie und Immunologie an der Universitat Hamburg, D-20251 Hamburg, Germany.. olaf.utermoehlen@medizin.uni-koeln.de) . Journal of virology, (2001 Nov) 75 (22) 10593-602. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB Protective immunity of BALB/c mice immunized with simian virus 40 (SV40) large T antigen (TAg) against SV40-transformed, TAg-expressing mKSA tumor cells is critically dependent on both CD8(+) and CD4(+) T lymphocytes. By depleting mice of T-cell subsets at different times before and after tumor challenge, we found that at all times, CD4(+) and CD8(+) cells both were equally important in establishing and maintaining a protective immune response. CD4(+) cells do not contribute to tumor eradication by **directly** lysing mKSA cells. However, CD4(+) lymphocytes provide help to CD8(+) cells to proliferate and to mature into fully active cytotoxic T lymphocytes (CTL). Depletion of CD4(+) cells by a single **injection** of CD4-specific monoclonal antibody at any time from **directly** before **injection** of the vaccinating antigen to up to 7 days after tumor challenge inhibited the generation of cytolytic CD8(+) lymphocytes. T helper cells in this system secrete the typical Th-1 cytokines interleukin 2 (IL-2) and gamma interferon. Because in this system TAg-specific CD8(+) cells secrete only minute amounts of IL-2, it appears that T helper cells provide these cytokines for CD8(+) T cells. Moreover, this helper effect of CD4(+) T cells in mKSA tumor rejection in BALB/c mice does not simply improve the activity of TAg-specific CD8(+) CTL but actually enables them to mature into cytolytic effector cells. Beyond this activity, the presence of T helper cells is necessary even in the late phase of tumor cell rejection in order to maintain protective immunity. However, despite the support of CD4(+) T helper cells, the tumor-specific **CTL response** is so weak that only at the site of tumor cell inoculation and not in the spleen or in the regional **lymph nodes** can TAg-specific CTL be detected.

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

1999:64705 Document No. 130:138281 A method of inducing a **CTL response.** Kundig, Thomas M.; Simard, John J. L. (CTL Immunotherapies Corporation, Can.). PCT Int. Appl. WO 9902183 A2 19990121, 199 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US14289 19980710. PRIORITY: CA 1997-2209815 19970710; US 1997-988320 19971210.

AB A method of inducing a cytotoxic T-lymphocyte (**CTL**) **response** to an antigen is disclosed. The method involves delivering the antigen to the lymphatic system of an animal regularly over a sustained period of time using, e.g., an osmotic pump. The method is advantageous over prior art methods for inducing a **CTL**

response in that it does not require repetitive immunizations or the use of adjuvants. The method of the present invention can be used for the induction of CTLs in tumor or infectious disease immunotherapy.

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=> s l2 and direct injection
L7          101 L2 AND DIRECT INJECTION

=> s l7 and lymph vessel
L8           10 L7 AND LYMPH VESSEL

=> dup remove l8
PROCESSING COMPLETED FOR L8
L9            9 DUP REMOVE L8 (1 DUPLICATE REMOVED)

=> d l9 1-9 cbib abs
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L9 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
2002:276188 Document No. 136:289366 Use of VEGF as a lymphangiogenic agents to treat lymphatic disorders. Gravereaux, Edwin C.; Silver, Marcy; Isner, Jeffrey M.; Yoon, Young-Sup (St. Elizabeth's Medical Center of Boston, Inc., USA). PCT Int. Appl. WO 2002029087 A2 20020411, 77 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US30904 20011002. PRIORITY: US 2000-PV237171 20001002.

AB The present invention provides methods for promoting the growth of new **lymph vessels** (lymphangiogenesis). Generally, such methods include administering at least one vascular endothelian factor (VEGF) such as VEGF-2. In one embodiment, therapeutic methods for treating lymphedema and related disorders in a human patient are disclosed. The VEGF can be provided by any suitable means including **direct injection** of a nucleic acid encoding same or an active fragment thereof. Also provided are pharmaceutical products for promoting lymphangiogenesis as well as a test system for screening compds. capable of inducing new **lymph vessel** growth. Addnl., the rabbit VEGFR-3 cDNA and protein are both claimed.

L9 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
2002:794299 Document No. 137:320695 Use of VEGFs as lymphangiogenic agents to treat lymphatic disorders. Gravereaux, Edwin C.; Silver, Marcy; Yoon, Young-sup; Isner, Jeffrey M.; Isner, Linda (St. Elizabeth's Medical Center of Boston, Inc., USA). U.S. Pat. Appl. Publ. US 2002151489 A1 20021017, 54 pp., Cont.-in-part of U. S. Provisional Ser. No. 237,171. (English). CODEN: USXXCO. APPLICATION: US 2001-970088 20011002. PRIORITY: US 2000-PV237171 20001002.

AB The present invention provides methods for promoting the growth of new **lymph vessels** (lymphangiogenesis). Generally, such methods include administering at least one vascular endothelian factor (VEGF) such as VEGF-2. In one embodiment, therapeutic methods for treating lymphedema and related disorders in a human patient are disclosed. The VEGF can be provided by any suitable means including **direct injection** of a nucleic acid encoding same or an active fragment thereof. Also provided are pharmaceutical products for promoting lymphangiogenesis as well as a test system for screening compds. capable of inducing new **lymph vessel** growth. Also provided are pharmaceutical products for promoting lymphangiogenesis as well as a test system for screening compds. capable of inducing new **lymph vessel** growth. Addnl., fragments of the rabbit VEGFR-3 cDNA and protein are both claimed.

L9 ANSWER 3 OF 9 MEDLINE on STN

2001653877. PubMed ID: 11706493. [Lymphadenography--pioneering work of Sven Bruun and Arnfinn Engeset]. Lymfadenografi--pionerarbeid av Sven Bruun og Arnfinn Engeset. Kolbenstvedt A. (Radiologisk avdeling Rikshospitalet 0027 Oslo.) Tidsskrift for den Norske laegeforening, (2001 Oct 10) 121 (24) 2836-7. Journal code: 0413423. ISSN: 0029-2001. Pub. country: Norway. Language: Norwegian.

AB Lymphadenography is a method for direct radiologic visualization of **lymph nodes** following injection of fat soluble contrast medium. Sven Bruun and Arnfinn Engeset at Rogaland Hospital developed this method in 1952 and published preliminary results in 1956. They have been somewhat overshadowed by the English surgeon John B. Kinmonth who published his method on lymphangiography in 1954. Kinmonth succeeded in visualizing the peripheral **lymph vessels** by **direct injection** of water soluble contrast medium. By this technique it was not feasible to depict **lymph nodes** above the knee because of diffusion of medium to surrounding tissues. Lymphography is a technique that visualizes both **lymph vessels** and **lymph nodes.** This method is based on a combination of the two above-mentioned methods with injection of fat soluble contrast medium into peripheral **lymph vessels.** Lymphography was a very important examination which was used all over the world in the 1960s and 1970s. It has now been replaced by other examinations.

L9 ANSWER 4 OF 9 EMBASE on STN

2000093020 EMBASE Lymphatic drainage of the heart and lungs in the pig: A preliminary study. Riquet M.; Hubsch J.P.; Chehab A.; Briere J.; Colomer S.; Hidden G.. Prof. M. Riquet, Laennec Hospital, Service de Chirurgie Thoracique, 42 rue de Sevres, 75007 Paris, France. riquet@lnc.ap-hop-paris.fr. European Journal of Lymphology and Related Problems 7/27 (80-84) 1999.

Refs: 17.

ISSN: 0778-5569. CODEN: EJLPE. Pub. Country: Belgium. Language: English. Summary Language: English.

AB In anatomy and physiology the pig is remarkably like man and is therefore considered as Potential Organ Donor. It was then particularly interesting to reconsider the lymphatic drainage of both its heart and lungs (H.L)Fifteen dead pigs were studied. The technique comprised removal of the sternocostal shield and injection into the myocardium and/or beneath the visceral pleura of a colored mass that was supplemented by **direct injection** of the nodes revealed in that manner. First colored nodes were tracheobronchial located-under the tracheal carina (ITBN), above the left (LSBN) and right (RSBN) main bronchus, above the right upper lobe tracheal bronchus (TBN) - and located at the lower level of the cervical trachea (CMN). There was no other pretracheal neither pulmonary LN contrary to human. The lymphatic vessels (LV) of the heart connected with the LSBN, rarely with the CMN. The LV issuing from : the ITBN connected with both the RSBN and LSBN and also with retrotracheal lymphcenter nodes (RTN); the RSBN connected with RTN, CMN or drained into the right jugulo subclavian venous confluent; The LSBN connected at times with RSBN and some lateroesophageal nodes, but generally drained into the left jugulosubclavian venous confluent, the arch of the thoracic duct (TD) and directly into the TD in the middle mediastinum, also an important lymph pathway in human. Lymphatics of the H.L. in pigs display anatomical patterns rarely observed in man but phylogeneticly explaining diseases as 'skipping' node metastases in lung cancer and chylothorax after heart and lungs surgery. In anatomy and physiology, the pig is remarkably like man. In 1966, Glauser underlined the advantages of Piglets as Experimental Animals in Pediatric Resarch : laboratory data comparing the newborn infant with the newborn piglet disclosed a striking similarity in the results reported for respiratory system. In adult research the pig's size proved to be a problem that was solved by breeding miniature pigs. Porcine

coronary arteries have almost the same pattern as the human being and investigators have found the pig particularly valuable for the study of coronary arteriosclerosis. The similitude between the 2 species are so great and the differences so little that since recently pig is considered as a potential organ donor and most of its organs are thought suitable for xenotransplantation. In view of contributing to such major topics, it seemed particularly interesting to reconsider the lymphatic drainage of both heart and lungs in this species so closely related to human.

L9 ANSWER 5 OF 9 MEDLINE on STN
93143457. PubMed ID: 1843434. [Anatomy and topography of external iliac **lymph nodes** in adults]. Anatomiia i topografiia naruzhnykh podvzdoshnykh limfaticheskikh uzlov u vzroslogo cheloveka. Shvetsov E V. Arkhiv anatomii, gistologii i embriologii, (1991 Jul-Aug) 100 (7-8) 50-7. Journal code: 0370603. ISSN: 0004-1947. Pub. country: RUSSIA: Russian Federation. Language: Russian.
AB The investigation of the external iliac **lymph nodes** has been performed in 152 preparations of corpses of mature persons of both sex, who died from causes not connected with any disease of the lymphatic system, lower extremities and pelvic organs. The external iliac **lymph nodes** and their afferent and efferent lymphatic vessels have been revealed by means of interstitial injection of the lower extremities and pelvic organs, as well as by means of **direct injection** of Gerota mass into the lymphatic vessels. Form, amount, dimensions and topography of common iliac **lymph nodes** have been studied. Lymphatic vessels, running from certain parts and organs of the body to various subgroups of the external iliac **lymph nodes** have been described, as well as efferent **lymph vessels** of these nodes. The external iliac **lymph nodes** are constant formations; the largest of them--**lymph nodes** of the lacuna--are nodes of the I step for the lower extremity **lymph vessels.** In 54% of cases in persons of both sex positive (right-sided) asymmetry has been revealed. Total amount of the iliac **lymph nodes** prevails in men, while their size is greater in women. The size of these nodes in persons of both sex is greater to the left than to the right. There are connections (in 3% of cases) between the external iliac **lymph nodes** and aortal and lumbar nodes of the opposite side.

L9 ANSWER 6 OF 9 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
1993:339492 Document No.: PREV199396036492. Anatomy and topography of external iliac **lymph nodes** in adults. Shvetsov, E. V.. Div. Anat. Human, I.M. Sechenov Mosc. Med. Acad., Moscow, Russia. Arkhiv Anatomii Gistologii i Embriologii, (1991) Vol. 100, No. 6-8, pp. 50-57. CODEN: AAGEAA. ISSN: 0004-1947. Language: Russian.
AB The investigation of the external iliac **lymph nodes** has been performed in 152 preparations of corpses of mature persons of both sex, who died from causes not connected with any disease of the lymphatic system, lower extremities and pelvic organs. The external iliac **lymph nodes** and their afferent and efferent lymphatic vessels have been revealed by means of interstitial injection of the lower extremities and pelvic organs, as well as by means of **direct injection** of Gerota mass into the lymphatic vessels. Form, amount, dimensions and topography of common iliac **lymph nodes** have been studied. Lymphatic vessels, running from certain parts and organs of the body to various subgroups of the external iliac **lymph nodes** have been described, as well as efferent **lymph vessels** of these nodes. The external iliac **lymph nodes** are constant formations; the largest of them - **lymph nodes** of the lacuna - are nodes of the I step for the lower extremity **lymph vessels.** In 54% of cases in persons of both sex positive (right-sided) asymmetry has been revealed. Total amount of the iliac **lymph nodes** prevails in men, while their size is greater in women. The size of these

nodes in persons of both sex is greater to the left than to the right. There are connections (in 3% of cases) between the external iliac **lymph nodes** and aortal and lumbar nodes of the opposite side.

L9 ANSWER 7 OF 9 MEDLINE on STN
84178034. PubMed ID: 6712496. [Anatomy and topography of the lymphatic vessels and regional **lymph nodes** of the rectum in newborn infants and children to 3 years of age]. Anatomiia i topografiia limfaticheskikh sosudov i regionarnykh limfaticheskikh uzlov priamoi kishki u novorozhdennykh i detei do 3 let zhizni. Abdykerimov S A. Arkhiv anatomii, gistologii i embriologii, (1984 Feb) 86 (2) 65-9. Journal code: 0370603. ISSN: 0004-1947. Pub. country: USSR. Language: Russian.
AB In 30 corpses of newborns and children up to 3 years of age, by means of the intratissue and **direct injection** of the modified Gerota's mass, certain increase in number and size of the superficial inguinal **lymph vessels** belonging to the superior-medial group, as well as the pararectal and superior rectal **lymph nodes** has been noted. The diameter of both afferent and efferent lymphatic vessels in the nodes mentioned in children of 1-3 years of age is greater than in the newborns. The number of the afferent vessels running towards these nodes in most cases, regardless the age, prevail over the efferent ones, and the diameter of the latter is greater than in the afferent vessels. The pararectal **lymph nodes** in 80% of cases are the nodes of the first step for the lymph flowing from the rectum, in 15% - the nodes of the first and second steps, simultaneously, and in 5% - of the third and fourth steps. The superior pararectal **lymph nodes** in 80% of cases are the nodes of the third and fourth steps, and in 20% of cases - those of the first and second steps for the lymph flowing from the rectum.

L9 ANSWER 8 OF 9 MEDLINE on STN DUPLICATE 1
83021796. PubMed ID: 7125916. [Variants in the number and size and the topography of the lumbar **lymph nodes** in the regional of the liver in the human adult]. Varianty kolichestva, razmerov i topografiia regionarnykh dlia pecheni poiasnichnykh limfaticheskikh uzlov u vzroslogoo cheloveka. Usovich A K; Borziak E I. Arkhiv anatomii, gistologii i embriologii, (1982 Jul) 83 (7) 29-33. Journal code: 0370603. ISSN: 0004-1947. Pub. country: USSR. Language: Russian.
AB By means of interstitial and **direct injections** of the lymphatic bed of the liver and gall bladder, their regional **lymph nodes** from the lumbar group have been studied in 63 corpses of mature persons of both sex. The hepatic **lymph vessels** flow into the lumbar **lymph nodes** in 73% of cases. Only the postaortal nodes (situating behind the abdominal part of the aorta) do not take the hepatic **lymph nodes.** The number of the hepatic regional lumbar **lymph nodes** varies from 1 to 6, and their size is within the limits 2X2--30X10 mm. In 13% of cases intercalated lumbar **lymph nodes** have been revealed (6X4 mm in size), they are situated along the pathway of the visceral surface of the **lymph vessels** (of the right hepatic lobe) running towards large intermediate lumbar **lymph nodes.**

L9 ANSWER 9 OF 9 EMBASE on STN
74210138 EMBASE Document No.: 1974210138. [**Lymph nodes** and lymphatics of the pelvis and the pelvic limb of the goat]. DIE LYMPHKNOTEN UND LYMPHGEFASSE DES BECKENS UND DER BECKENGLIEDMASSE DER ZIEGE. Roos H.; Frewein J.. Inst. Makrosk. Anat. Tiere, Univ. Munchen, Germany. BERL.MUNCH.TIERARZTL.WSCHR. 87/6 (101-105) 1974. CODEN: BEMTAM. Language: German.
AB The **lymph nodes** of the pelvis and the pelvic limb were examined in 46 goats of different breeds and different ages. Many of the afferent lymphatics were visualized by injection of a mixture of Indian

ink and water or Indian ink and serum into the subcutis, into fascias, tendons, tendon sheaths, joint capsules and ligaments. The efferent lymphatics were filled by **direct injection** into the **lymph nodes.** The following **lymph nodes** are always present: Ln. popliteus, Ln. ischiadicus, Ln. inguinalis superficialis, Ln. subiliacus, Lnn. iliaci mediales, and Ln. sacralis. Not always present are: Ln. tuberalis Ln. inguinalis profundus, and Ln. hypogastricus.

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FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 14:05:25 ON 12 MAY 2004

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L1             0 S FOLICLE INJECTION
L2        354385 S LYMPH NODE
L3         20700 S L2 AND INJECTION
L4           192 S L3 AND CTL RESPONSE
L5            11 S L4 AND DIRECTLY
L6             3 DUP REMOVE L5 (8 DUPLICATES REMOVED)
L7           101 S L2 AND DIRECT INJECTION
L8            10 S L7 AND LYMPH VESSEL
L9             9 DUP REMOVE L8 (1 DUPLICATE REMOVED)

=> s l7 and CTL response
L10            0 L7 AND CTL RESPONSE

=> s l7 and tumor
L11           27 L7 AND TUMOR

=> dup remove l11
PROCESSING COMPLETED FOR L11
L12           13 DUP REMOVE L11 (14 DUPLICATES REMOVED)

=> d l12 1-13 cbib abs
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L12 ANSWER 1 OF 13 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

2004113784 EMBASE Optimised nuclear medicine method for tumour marking and sentinel node detection in occult primary breast lesions. De Cicco C.; Trifiro G.; Intra M.; Marotta G.; Ciprian A.; Frasson A.; Prisco G.; Luini A.; Viale G.; Paganelli G.. C. De Cicco, Division of Nuclear Medicine, European Institute of Oncology, University of Milan, Via Ripamonti, 435-20141 Milan, Italy. concetta.de-cicco@ieo.it. European Journal of Nuclear Medicine and Molecular Imaging 31/3 (349-354) 2004.
Refs: 17.
ISSN: 1619-7070. CODEN: EJNMA6. Pub. Country: Germany. Language: English. Summary Language: English.

AB The aim of this study was to evaluate the feasibility of sentinel node (SN) biopsy in occult breast lesions with different radiopharmaceuticals and to establish the optimal lymphoscintigraphic method to detect both occult lesions and SNs (SNOLL: sentinel node and occult lesion localisation). Two hundred and twenty-seven consecutive patients suspected to have clinically occult breast carcinoma were enrolled in the study. In addition to the radioguided occult lesion localisation (ROLL) procedure, using macroaggregates of technetium-99m labelled human serum albumin (MAA) injected directly into the lesion, lymphoscintigraphy was performed with nanocolloids (NC) injected in a peritumoral (group I) or a subdermal site (group II). In group III, a sole injection of NC was done into the lesion in order to perform both ROLL and SNOLL. Overall, axillary SNs were identified in 205 of the 227 patients (90.3%). In 12/62 (19.4%) patients of group I and 9/79 (11.4%) patients of group III, radioactive nodes were not visualised, whereas SNs were successfully localised in 85 of 86

patients of group II (P<0.001). Pathological findings revealed breast carcinoma in 148/227 patients (65.2%) and benign lesions in 79 (34.8%). A total of 131 axillary SNs were removed in 118 patients with breast carcinoma; intraoperative examination of the SNs revealed metastatic involvement in 16 out of 96 cases of invasive c arcinoma (16.7%). It is concluded that the combination of the ROLL procedure with **direct injection** of MAA into the lesion and lymphoscintigraphy performed with subdermal injection of radiocolloids represents the method of choice for accurate localisation of both non-palpable lesions and SNs.

L12 ANSWER 2 OF 13 MEDLINE on STN DUPLICATE 1

2002383730. PubMed ID: 12133274. Oncolytic herpesvirus effectively treats murine squamous cell carcinoma and spreads by natural lymphatics to treat sites of lymphatic metastases. Wong Richard J; Joe John K; Kim Se-Heon; Shah Jatin P; Horsburgh Brian; Fong Yuman. (Head and Neck Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY 10021, USA.) Human gene therapy, (2002 Jul 1) 13 (10) 1213-23. Journal code: 9008950. ISSN: 1043-0342. Pub. country: United States. Language: English.

AB Oncolytic herpesviruses have significant antitumoral effects in animal models when delivered directly to established **tumors.** Lymphatic metastases are a common occurrence for many **tumor** types. This study investigates the potential of an attenuated, replication-competent, oncolytic herpes simplex virus (NV1023) both to treat a primary **tumor** by **direct injection** and to travel through the lymphatic system to treat metastatic **tumor** within the **lymph nodes** draining lymph from the site of primary cancer. Isosulfan blue dye was injected into murine auricles to determine normal lymphatic drainage patterns and demonstrated consistent blue staining of a group of ipsilateral cervical **lymph nodes.** Auricular injections of NV1023 resulted in viral transit to these **lymph nodes** as measured by 5-bromo-4-chloro-3-indolyl-beta-D-galactopyranoside histochemistry and viral plaque assay. An oncolytic herpesvirus (NV1066) expressing green fluorescent protein also demonstrated viral transit from the auricle to the cervical **lymph nodes** on fluorescence microscopy. Using the SCC VII cell line, a novel murine model of auricular squamous cell carcinoma was developed with an approximately 20% incidence of cervical **lymph node** metastases. Delivery of NV1023 or NV1066 to the surgical beds after excision of auricular SCC VII **tumors** resulted in successful viral infection of metastatic SCC VII cells within the cervical **lymph nodes.** After a 7-week follow-up, significantly enhanced locoregional control ($p < 0.05$, Fisher exact test) and disease-free survival ($p < 0.05$, log rank test) were evident with NV1023 treatment. This study demonstrates that the delivery of an oncolytic herpesvirus to a primary **tumor** site after surgical excision may have a significant impact on reducing both primary site recurrence and regional nodal metastases.

L12 ANSWER 3 OF 13 MEDLINE on STN DUPLICATE 2

2002182449. PubMed ID: 11916241. Suppression of murine mammary carcinoma growth and metastasis by HSVtk/GCV gene therapy using in vivo electroporation. Shibata Masa-Aki; Morimoto Junji; Otsuki Yoshinori. (Department of Anatomy and Biology, Osaka Medical College, Takatsuki, Japan.) Cancer gene therapy, (2002 Jan) 9 (1) 16-27. Journal code: 9432230. ISSN: 0929-1903. Pub. country: England: United Kingdom. Language: English.

AB The effectiveness of electroporation as a means of gene transfection, both in vitro and in vivo, was tested using the herpes simplex virus 1 thymidine kinase (HSVtk) gene in combination with ganciclovir (GCV) administration as therapy against murine mammary cancer. Approximately 80% of BJMC3879 metastatic mammary carcinoma cells, derived from MMTV-infected BALB/c mice, died as a result of HSVtk/GCV treatment 72 hours after the transfection; decreased DNA synthesis was also seen. Mammary **tumors** induced by inoculation of syngeneic mice with

BJMC3879 cells were subsequently treated by **direct injection** of vector containing HSVtk (pHSVtk) alone, empty vector or saline alone twice a week. After each injection, the **tumors** were subjected to in vivo electroporation. Mice treated with pHSVtk or saline were intraperitoneally injected with GCV at 40 mg/kg five times a week. Significantly reduced **tumor** volumes were observed for the pHSVtk+GCV group in experimental week 2 and thereafter throughout the 2-month study. DNA synthesis was significantly decreased as well in the pHSVtk+GCV group compared with all other groups. Furthermore, metastasis to **lymph nodes** and lungs was significantly suppressed by HSVtk/GCV treatment. Expression of HSVtk in the **tumors** was confirmed by RT-PCR. Macrophage accumulations were frequently observed in the peripheries of necrotic regions in HSVtk/GCV-treated **tumors**, where levels of apoptosis were significantly higher than those observed in other groups. We therefore conclude that in vivo electroporation can result in efficient gene transfer and that the HSVtk/GCV prodrug system strongly suppresses **tumor** growth and metastases in this model.

L12 ANSWER 4 OF 13 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
1999:625155 The Genuine Article (R) Number: 224AQ. Distribution of retroviral vectors and vector producer cells using two routes of administration in rats. Kaloss M; Linscott M; Wey C; Lu P; Long Z; McGarrity G J; Otto E; Lyons R M (Reprint). GENET THERAPY INC, 938 CLOPPER RD, GAITHERSBURG, MD 20878 (Reprint); GENET THERAPY INC, GAITHERSBURG, MD 20878. GENE THERAPY (AUG 1999) Vol. 6, No. 8, pp. 1389-1396. Publisher: STOCKTON PRESS. HOUNDMILLS, BASINGSTOKE RG21 6XS, HAMPSHIRE, ENGLAND. ISSN: 0969-7128. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The clinical use of retroviral vector producer cells (VPCs) to deliver retroviral vectors efficiently to target cells has been investigated as a method to increase efficiency of gene delivery, presumably as a result of continued vector production in vivo. Studies were conducted in rats to evaluate the distribution of vector to distal organs and tissues as measured by transduction. Rats were treated with two doses of VPCs using two routes of administration: (1) subcutaneous injection, chosen to maximize both the dose and exposure of animals, thereby enabling identification of potential target organs under worst-case conditions; and (2) **direct injection** into brain parenchyma, chosen to mimic the intended clinical route of administration and provide an estimate of risk to patients receiving this therapy. Twelve organs or tissues were collected 7 days after administration of VPCs and analyzed by PCR for the presence of vector and vector producer cell sequences. Vector was detected most frequently at the site of injection by either route of administration. Less frequently, vector was detected in draining **lymph nodes** at the higher dose only using either route of injection. Single specimens of lung and contralateral skin were positive for vector following subcutaneous administration only. Vector was detected in gonadal tissue from a single low-dose male following subcutaneous administration, but this finding was not reproduced in any high-dose male or any males injected intracerebrally. In contrast, VPCs were detected only at the site of administration. The frequency of detection of VPCs 7 days after administration was higher when rats were injected by the intracerebral route. Based on these studies, gene transfer to distal organs or gonadal tissue following intracerebral administration of VPCs is not considered to be a risk to patients undergoing retroviral Vector gene therapy for the treatment of brain cancer (glioblastoma multiforme; GBM).

L12 ANSWER 5 OF 13 MEDLINE on STN DUPLICATE 3
1998033894. PubMed ID: 9367025. Cytokines as an adjuvant to **tumor** vaccines: efficacy of local methods of delivery. Kurane S; Arca M T; Aruga A; Krinock R A; Krauss J C; Chang A E. (Division of Surgical Oncology, University of Michigan, Ann Arbor, USA.) Annals of surgical oncology : official journal of the Society of Surgical Oncology, (1997 Oct-Nov) 4 (7) 579-85. Journal code: 9420840. ISSN: 1068-9265. Pub. country: United

States. Language: English.

AB BACKGROUND: We examined alternative methods of delivering cytokines as an adjunct for priming **lymph node** (LN) cells draining sites of vaccine inoculation for the purpose of generating immune cells for adoptive immunotherapy. METHODS: Using syngeneic murine **tumors** we examined the ability of IL-2, IL-4, or GM-CSF delivered locally to a site of **tumor** inoculum to induce antitumor reactive draining LN cells. Mice were inoculated subcutaneously with **tumor** cells transduced to secrete cytokine; **tumor** cells admixed with fibroblasts transduced to secrete cytokine; or intralesional inoculation of cytokine in established **tumor** to induce sensitized LN cells capable of mediating **tumor** regression in adoptive transfer. RESULTS: Both IL-4 and GM-CSF cytokines were effective in enhancing the antitumor reactivity of vaccine-primed LN cells compared to IL-2, which was ineffective. The local delivery of GM-CSF by autocrine or paracrine secretion of genetically engineered cells, as well as direct intratumoral delivery was capable of upregulating LN sensitization compared to systemic administration, which did not. CONCLUSIONS: The local delivery of GM-CSF as an adjuvant for **tumor** vaccination can be accomplished by various methods, including **direct injection**, which avoids the need for gene transfer.

L12 ANSWER 6 OF 13 MEDLINE on STN DUPLICATE 4

97159158. PubMed ID: 9006499. A new immunocompetent murine model for oral cancer. O'Malley B W Jr; Cope K A; Johnson C S; Schwartz M R. (Department of Otolaryngology-Head and Neck Surgery, Johns Hopkins University, Baltimore, Md, USA.) Archives of otolaryngology--head & neck surgery, (1997 Jan) 123 (1) 20-4. Journal code: 8603209. ISSN: 0886-4470. Pub. country: United States. Language: English.

AB OBJECTIVE: To develop and characterize a new immunocompetent murine model that attempts to parallel the clinical and biological nature of head and neck cancer. DESIGN: The growth rate and histologic characteristics of the SCC VII/SF cell line were initially determined in tissue culture experiments. Animal experiments were subsequently performed on C3H/HeJ mice. Using **direct injection**, 5 x 10(5) SCC VII/SF cells were delivered to the floor of the mouth of each animal. Animals were killed after 1, 2, and 3 weeks, and **tumor** growth, invasion, and regional and distant metastases were evaluated. RESULTS: Squamous cell carcinomas that could be palpated and measured externally were identified in the floor of the mouth of C3H/HeJ mice after 5 to 7 days. Local invasion into the mylohyoid musculature and mandible was present. Cervical **lymph node** and pulmonary metastases were identified between 2 and 3 weeks. CONCLUSIONS: This study introduces a new oral cancer animal model that shows initial locoregional **tumor** invasion, direct extension into the neck, early cervical metastases, and pulmonary metastases. These clinical and histopathologic attributes reflect the biological behavior and **tumor** progression seen in human oral cancer and therefore provide a model for clinically applicable research for primary and metastatic head and neck cancer.

L12 ANSWER 7 OF 13 EMBASE on STN

95288854 EMBASE Document No.: 1995288854. Locoregional immunotherapy - Topics at the 13th and 14th meeting of the Japanese Research Society for Surgical Cancer Immunology. Amano S.; Kurosu Y.; Shibata M.. First Department of Surgery, Nihon University School of Medicine, 30-1 Oyaguchi-Kamimachi,Itabashi-ku, Tokyo 173, Japan. Biotherapy 9/7 (845-851) 1995. ISSN: 0914-2223. CODEN: BITPE. Pub. Country: Japan. Language: Japanese. Summary Language: English; Japanese.

AB Seventy papers concerning locoregional immunotherapy were presented at the 1992.apprx.1993 meetings. The subjects were head and neck cancer, breast cancer, lung cancer, gastric cancer, liver cancer, colon cancer, metastatic cancer, peritonitis carcinomatosa and experimental animal **tumors.** The methods of administration of BRMs were **direct injection** into the **tumor** or the regional **lymph**

nodes, or infusion into the hepatic artery or portal vein. Various BRMs were used (OK-432, PSK lentinan, IL-2, TNF, IFN-γ, and mono-clonal antibody, such as missile therapy). New and hopeful challenges have been launched to overcome cancer growth, using the new techniques developed in the field of molecular biology, for example.

L12 ANSWER 8 OF 13 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
93:661637 The Genuine Article (R) Number: MD940. A GENETIC APPROACH TO IDIOTYPIC VACCINATION. HAWKINS R E (Reprint); WINTER G; HAMBLIN T J; STEVENSON F K; RUSSELL S J. MRC, MOLEC BIOL LAB, HILLS RD, CAMBRIDGE CB2 2HQ, ENGLAND (Reprint); CTR PROT ENGN, CAMBRIDGE, ENGLAND; TENOVUS LAB, MOLEC IMMUNOL GRP, SOUTHAMPTON, ENGLAND. JOURNAL OF IMMUNOTHERAPY (NOV 1993) Vol. 14, No. 4, pp. 273-278. ISSN: 1053-8550. Pub. country: ENGLAND. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Treatment of cancer with vaccines is an attractive prospect, but few tumours express suitable target antigens. With B-cell lymphomas, the idiotypic immunoglobulin (Ig) of the malignant B-cell should provide a suitable target but this requires a vaccine to be created for each patient. We propose a strategy for making such vaccines: first to clone the V genes of the idiotypic Ig, and second to inject the patient with the cloned DNA (genetic immunisation) in order to elicit an immune response against the encoded Ig. We have previously shown that the V genes of the idiotypic Ig can be identified from human **lymph node** biopsies by polymerase chain reaction amplification, cloning, and sequencing. In this report, we show that anti-idiotypic antibodies can be elicited by **direct injection** of an expression vector that encodes the V genes of murine antibodies (the V genes of B1.8, a murine hybridoma or of BCL1, a murine lymphoma line).This finding suggests a simple approach to the preparation of idiotypic vaccines for patients with B-cell lymphoma, which also circumvents the need for adjuvants.

L12 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
1993:465 Document No. 118:465 Study on immune response of lymphocytes in the regional **lymph nodes** of gastric cancer by **direct injection** of active charcoal-adsorbed β (1→3) glucan. Shibata, Kazunari; Suzuki, Kazunobu; Tsurui, Shigeru; Tanifuji, Kiminori (Dep. Surg., Tokyo Med. Coll., Tokyo, Japan). Tokyo Ika Daigaku Zasshi, 50(3), 443-53 (Japanese) 1992. CODEN: TIDZAH. ISSN: 0040-8905.
AB Via an endoscope, active charcoal-adsorbed lentinan, lentinan, and active charcoal were locally applied to foci in 65 patients with curatively resectable gastric cancer before surgery, in an attempt to improve antitumoral activity of lymphocytes on the regional **lymph nodes** and to prevent malignant disease course progression. The resulting immune response was then evaluated by determining the functions of **lymph nodes** by measuring the ratio of the composition of various T cell subgroups, IL-2 production, LAK cell activity, and NK cell activity. Lentinan reinforced with adsorptive active charcoal particles had superior high lymph specificity and exerted a slow-release effect by accumulating in the regional **lymph nodes** via the lymph flow. In addition, this type of lentinan proved more effective than locally or systemically applied lentinan for increasing the immunol. competence of group I **lymph nodes** and raising lymphocyte antitumoral activity. Thus, supplementing lentinan with adsorptive active charcoal particles and locally applying it may be effective for preventing **tumor** metastasis.

L12 ANSWER 10 OF 13 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
1986:418611 Document No.: PREV198682094145; BA82:94145. THE ROLE OF THE PEYER'S PATCH IN CARCINOGENESIS I. THE ADSORPTION FROM THE GUT AND RETENTION OF 3 METHYLCHOLANTHRENE BY PEYER'S PATCHES. BOST K L [Reprint author]; CUCHENS M A. DEP OF MICROBIOL, UNIV OF MISSISSIPPI MED CENT, 2500 N STATE ST, JACKSON, MS 39216, USA. Carcinogenesis (Oxford), (1986) Vol. 7, No. 8, pp. 1251-1256.

CODEN: CRNGDP. ISSN: 0143-3334. Language: ENGLISH.

AB Radiotracer methods were used to determine the distribution of 3-methylcholanthrene (3-MC) within the lymphoid organs of rats followingi.g. intubation, i.l. injection into the small intestine, i.v. injection or **direct injection** of the Peyer's patches with 3-[6-14C]methylcholanthrene (14C-MC). The data indicate that the gut-associated Peyer's patches and mesenteric **lymph nodes** were exposed to higher amounts of orally administered 14C-MC than any of the other lymphoid organs. Whereas the Peyer's patches exhibited the highest sp. act. for longer periods of time when low amounts of 14C-MC were administered, the sp. act. of the mesenteric **lymph node** were greater when rats were intubated with higher amounts of 14C-MC. Furthermore, the Peyer's patches were exposed to higher amounts of possible metabolites of 14C-MC. Injection of 14C-MC into the small intestinal lumen resulted in increased ratios of the Peyer's patch sp. act. to mesenteric **lymph node** sp. act., indicating that by-passing the stomach altered the distribution patterns. Data from rats injected i.v. with 14C-MC demonstrated that mesenteric **lymph nodes** but not Peyer's patches adsorbed and retained 14C-MC from the blood and indicated that the 14C-MC associated with Peyer's patches of i.g. treated rats was adsorbed from the gut rather than from the blood. Results obtained from rats which were exposed to 3-MC by directly injecting Peyer's patches with 14C-MC also indicated that the Peyer's patches were able to retain 3-MC once localized within this lymphoid organ, to metabolize the 3-MC and to possibly excrete the polycyclic aromatic hydrocarbon into the small intestine. Collectively the data indicate that Peyer's patches have an important role in the adsorption from the gut and subsequent retention of 3-MC and hence may be a likely target organ for lymphoid carcinogenesis following oral exposure to carcinogenic polycyclic aromatic hydrocarbons.

L12 ANSWER 11 OF 13 MEDLINE on STN DUPLICATE 5

86105673. PubMed ID: 3943008. Salvage of stage IV intraoral squamous cell carcinomas with preoperative 5-fluorouracil. Ryan R F; Krementz E T; Truesdale G L. Cancer, (1986 Feb 15) 57 (4) 699-705. Journal code: 0374236. ISSN: 0008-543X. Pub. country: United States. Language: English.

AB A regimen for improving the salvage rate for Stage IV squamous cell carcinoma of the tongue, alveolar ridge and floor of mouth is presented. This method utilizes pre-operative sensitization of the **tumor** and regional **lymph nodes** by the topical application of 5-fluorouracil (5-FU) in the form of Efudex (Roche). The drug must be used topically at the **tumor** skin or **tumor**-mucous membrane interface to utilize the sensitizing properties of skin or mucous membrane. Further response is obtained by **direct injections** of 5-FU into the **tumor.** Later intravenous (IV) drip of 5-FU can be used particularly at the time of surgical resection. During the period of preparation until sensitized to 5-FU, patients must be restored to positive nitrogen balance and concurrent infections are controlled. Because of the importance of nutrition in restoring immunity, a feeding gastrostomy for these patients is recommended. The definitive surgery must include all bone that is involved, as 5-FU alone will not sterilize the bone. Of 15 patients who underwent the regimen outlined in this study, 12 of the patients with Stage IV intra-oral squamous cell carcinoma have had their primary **tumor** controlled for 17 months to 5 years at the time of this report.

L12 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

1984:79567 Document No. 100:79567 Experimental study of local chemotherapy with topical injection of adriamycin. Muto, Fumitaka (1st Dep. Surg., Kyoto Prefect. Univ. Med., Kyoto, Japan). Kyoto-furitsu Ika Daigaku Zasshi, 92(12), 2027-36 (Japanese) 1983. CODEN: KFIZAO. ISSN: 0023-6012.

AB Local application of adriamycin [23214-92-8] is more efficient than i.v. injection in controlling **lymph node** metastasis and minimizing toxic side effects. This was demonstrated by injecting the

drug into rat gastric mucosa and showing a high concentration of the drug in the stomach for a prolonged period with little toxic effect on the stomach. The concentration of adriamycin in the liver was considerably less than that observed after i.v. injection. In rats bearing AH-130 **tumor** in the foot pad, **direct injection** of adriamycin into the **tumor** increased the survival rate and had a greater efficacy than did the i.v. injection.

L12 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
1949:15666 Document No. 43:15666 Original Reference No. 43:3095b-e The development of **tumors** in various tissues in mice following direct application of a carcinogenic hydrocarbon. Rask-Nielsen, Ragna Acta Path. Microbiol. Scand., Suppl., 78, 1-144 (Unavailable) 1948.
AB **Direct injection** of a small amount of 9,10-dimethyl-1,2-benzanthracene into various organs of mice indicates that the thymus gland and lung are more susceptible than any of the other tissues which produce **tumors** spontaneously (subcutaneous tissue, skin, mammary tissue). **Direct injection** of large doses of this carcinogen into various organs induced **tumors** in thymus gland, lung, and also subcutaneous tissue but not in the other tissues capable of spontaneous **tumor** formation, or in those not capable of spontaneous **tumor** formation (**lymph nodes**, spleen, bone marrow, kidney and testis) with the exception of one testicular sarcoma. Nonlocal **tumor** formation was observed in thymus gland and lung, with leukemic infiltration only, in **lymph nodes** and spleen. Carcinogenic agents do not produce **tumors** in tissues incapable of the spontaneous generation of **tumors.**

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=> s CTL response
L13      14984 CTL RESPONSE

=> s l13 and direct injection
L14         27 L13 AND DIRECT INJECTION

=> s l14 and lymph node
L15          0 L14 AND LYMPH NODE

=> s l14 and lymph vessel
L16          0 L14 AND LYMPH VESSEL

=> dup remove l14
PROCESSING COMPLETED FOR L14
L17           7 DUP REMOVE L14 (20 DUPLICATES REMOVED)

=> d l17 1-7 cbib abs

L17 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
2004:313774 Enhancement of HBV gene-induced specific cell-mediated
     immunoresponse by C3d-P28. Wang, Lixin; Xu, Wei; Guan, Qingdong; Xiong,
     Sidong (Shanghai Medical College, Fudan University, Shanghai, 200032,
     Peop. Rep. China). Xibao Yu Fenzi Mianyixue Zazhi, 19(3), 242-244
     (Chinese) 2003. CODEN: XFMZFM. ISSN: 1007-8738. Publisher: Xibao Yu
     Fenzi Mianyixue Zazhi Bianjibu.
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AB To investigate whether P28 derived from complement C3d can enhance the cell-mediated immunoresponse to HBV-preS2/S induced by **direct injection** of naked plasmid DNA containing four tandem repeats of C3d-P28 gene and HBV-preS2/S gene existed in fusion form. Four copies of gene coding for C3d-P28, amplified by PCR and cut by restriction endonucleases digestion, were subcloned into a eukaryotic expression vector pVAON33 to construct pVAON33-P28.4. HBV-preS2/S gene was then introduced into the pVAON33 and pVAON33-P28.4 resp. to form pVAON33-S2/S and pVAON33-S2/S-P28.4. The recombinant plasmids were identified by PCR

and restriction endonucleases digestion as well as DNA sequencing. BALB/c mice were immunized I.m. three times at 3 wk' intervals with 100 μg of pVAON33-S2/S DNA, pVAON33-S2/S-P28.4 and mock DNA, resp. Splenocytes from immunized mice were stimulated by HBsAg and then harvested to analyze the specific lymphocytic proliferative response and CTL cytotoxic activity by 3H-TdR incorporation assay and isotopic release anal., resp. Specific lymphocytic proliferation and CTL cytotoxic activity against HBV-preS2/S were observed in mice immunized by both pVAON33-S2/S and pVAON33-S2/S-P28.4 in dose-dependent form. Specific lymphocytic proliferation and **CTL response** in mice immunized by pVAON33-S2/S-P28.4 were markedly stronger than those in mice immunized by pVAON33-S2/S. A C3d-P28 can enhance the cell-mediated immunoresponse induced by HBV-preS2/S gene immunization.

L17 ANSWER 2 OF 7 MEDLINE on STN DUPLICATE 1

2000031176. PubMed ID: 10566900. RNA melanoma vaccine: induction of antitumor immunity by human glycoprotein 100 mRNA immunization. Zhou W Z; Hoon D S; Huang S K; Fujii S; Hashimoto K; Morishita R; Kaneda Y. (Division of Gene Therapy Science, Osaka University School of Medicine, Suita, Japan.) Human gene therapy, (1999 Nov 1) 10 (16) 2719-24. Journal code: 9008950. ISSN: 1043-0342. Pub. country: United States. Language: English.

AB An RNA melanoma vaccine was investigated to induce protective immunity in a mouse-melanoma model. LacZ mRNA was synthesized in vitro by pSFV3 expression vector and introduced into the spleen of mice, using HVJ-liposomes. A high level of beta-galactosidase activity was detected for 10 days in mouse spleen. The human melanoma-associated antigen gp100 mRNA was synthesized in vitro by pSFV3 vector and encapsulated in HVJ-liposomes. Immunization by **direct injection** of the gp100 mRNA HVJ-liposomes into mouse spleen induced both anti-gp100 Ab and **CTL responses** against B16 melanoma. Immunization by administration of gp100 mRNA into the spleen delayed tumor growth and significantly prolonged survival compared with control treated mice. These preclinical studies demonstrate that an RNA tumor antigen vaccine strategy has potential application for human cancer treatment and prevention.

L17 ANSWER 3 OF 7 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

1999:224191 The Genuine Article (R) Number: 175YD. Enhanced cellular immunity to hepatitis C virus nonstructural proteins by codelivery of granulocyte macrophage-colony stimulating factor gene in intramuscular DNA immunization. Cho J H; Lee S W; Sung Y C (Reprint). POHANG UNIV SCI & TECHNOL, SCH ENVIRONM ENGN, CTR BIOFUNCT MOL, DEPT LIFE SCI, SAN 31, POHANG 790784, KYUNGBUK, SOUTH KOREA (Reprint); POHANG UNIV SCI & TECHNOL, SCH ENVIRONM ENGN, CTR BIOFUNCT MOL, DEPT LIFE SCI, POHANG 790784, KYUNGBUK, SOUTH KOREA. VACCINE (5 MAR 1999) Vol. 17, No. 9-10, pp. 1136-1144. Publisher: ELSEVIER SCI LTD. THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND. ISSN: 0264-410X. Pub. country: SOUTH KOREA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Hepatitis C virus (HCV) nonstructural (NS) proteins appeared to be important targets for HCV vaccine development, since NS-specific T-helper-cell responses are associated with clearance from acute HCV infection. In this report, we have constructed a plasmid, pTV-NS345, that encodes the HCV NS3, NS4 and NS5 proteins (NS345) and a bicistronic plasmid, PIV-NS345/GMCSF, in which the HCV NS345 polyprotein and GMCSF are translated independently. Intramuscular inoculation with pTV-NS345 plasmid DNA into the Buffalo rats generated both antibody and T-cell proliferative responses to each NS protein. The expression of GMCSF, together with HCV NS345 proteins, appeared to significantly increase T-cell proliferative responses. In particular, the inoculation of a bicistronic plasmid generated higher T-cell proliferative responses to each NS protein than did the coinjection of two separate plasmids, pTV-NS345 and pTV-GMCSF. These results demonstrate that the codelivery of GMCSF augmented HCV NS345-specific cellular immunity and that the intensity of the immunity

was differed depending on how GMCSF gene is codelivered. (C) 1999 Elsevier Science Ltd. All rights reserved.

L17 ANSWER 4 OF 7 MEDLINE on STN DUPLICATE 2

1998286926. PubMed ID: 9625262. Similarity of strain- and route-dependent murine responses to an adenovirus vector using the homologous thrombopoietin cDNA as the reporter genes. Suzuki M; Singh R; Moore M A; Song W R; Crystal R G. (Division of Pulmonary and Critical Care Medicine, The New York Hospital-Cornell Medical Center, NY 10021, USA.) Human gene therapy, (1998 May 20) 9 (8) 1223-31. Journal code: 9008950. ISSN: 1043-0342. Pub. country: United States. Language: English.

AB Replication-deficient adenovirus (Ad) vectors are effective in transferring genes in vivo, but their use is associated with significant variation in the extent and/or duration of expression observed among different strains of experimental animals and different routes of administration of the vector. We have minimized the variables of the heterologous transgene and animal-to-animal variation by constructing an Ad vector encoding murine thrombopoietin (mTPO, AdmTPO), a homologous protein that induces a physiologic response (elevation of blood platelet levels) that can be followed sequentially over time in the same animal. Using the C57BL/6 and BALB/c stains, liver administration was accomplished by intravenous administration and skeletal muscle administration by **direct injection.** Despite the use of a homologous cDNA as a transgene, the Ad genome was rapidly lost from the liver after intravenous administration over the first 1 to 2 weeks, with no difference in pattern of decline between the C57BL/6 and BALB/c strains. Both strains exhibited a cytotoxic T lymphocyte (**CTL**) **response** directed against the AdmTPO vector. Consistent with the decline in vector genome over time, the initial high levels of mTPO mRNA in the liver declined to an undetectable level within 2 weeks. Platelet counts peaked at 8- to 10-fold above baseline within the first 2 weeks, and then gradually declined, returning to normal level by 50 to 60 days. Intravenous administration of the AdmTPO vector to beta2-microglobulin-deficient mice resulted in a longer persistence of elevated platelets levels, although the eventual return of platelet levels to normal in these mice suggests the elimination of the Ad vector cannot be explained solely by **CTL response.** Although the intramuscular administration of the AdmTPO vector resulted in platelet levels with a lower peak and minor differences over time compared with the intravenous route, the C57BL/6 and BALB/c strains demonstrated the same rapid loss of Ad genome and mTPO mRNA levels in the muscle as in the liver. Together, these observations suggest that simplifying the experimental design by eliminating the variable of host response to a heterologous transgene, and by following the consequences of gene transfer in the same animals over time, there can be remarkable similarity in strain- and route-dependent responses to an Ad vector.

L17 ANSWER 5 OF 7 MEDLINE on STN DUPLICATE 3

96234392. PubMed ID: 8640771. Protection against a lethal challenge with SV40-transformed cells by the **direct injection** of DNA-encoding SV40 large tumor antigen. Bright R K; Beames B; Shearer M H; Kennedy R C. (Department of Virology and Immunology, Southwest Foundation for Biomedical Research, San Antonio, Texas 78228, USA.) Cancer research, (1996 Mar 1) 56 (5) 1126-30. Journal code: 2984705R. ISSN: 0008-5472. Pub. country: United States. Language: English.

AB Plasmid DNA encoding the large tumor antigen (T- ag) of SV40 was used to actively immunize mice to assess the induction of SV40 T-ag-specific immunity. Mice were injected with the naked DNA i.m., and immune responses were compared to those elicited in mice immunized with the recombinant SV40 T-ag protein. Compared to immunization with the recombinant protein, naked DNA induced weak antibody responses to SV40 T-ag. No increase in natural killer cell activity was observed following either recombinant protein or nucleic acid vaccination. However, the recombinant SV40 T-ag failed to induce SV40 T-ag-specific **CTL responses**, whereas the plasmid DNA encoding SV40 T-ag elicited CTL

activity specific for SV40 T-ag. The SV40 T-ag-specific CTL lysed in vitro only syngeneic target cells (H-2(d)) expressing SV40 T-ag, indicating that the CTL are MHC restricted. Both the recombinant protein and naked DNA preparations induced immune responses that were protective against a lethal challenge with syngeneic SV40-transformed cells. A comparison of recombinant protein versus nucleic acid immunization indicates that both humoral and cell-mediated immune responses may play a role in SV40 T-ag immunity. These data indicate that active immunization with genes encoding tumor-specific antigens may be an efficacious strategy for the induction of tumor immunity.

L17 ANSWER 6 OF 7 MEDLINE on STN DUPLICATE 4
96020094. PubMed ID: 7492440. Induction of potent humoral and cell-mediated immune responses following **direct injection** of DNA encoding the HIV type 1 env and rev gene products. Okuda K; Bukawa H; Hamajima K; Kawamoto S; Sekigawa K; Yamada Y; Tanaka S; Ishi N; Aoki I; Nakamura M. (Department of Bacteriology, Yokohama City University School of Medicine, Japan.) AIDS research and human retroviruses, (1995 Aug) 11 (8) 933-43. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB DNA vaccines have the potential of giving rise to a potent cell-mediated immune response by inducing intracellular synthesis and subsequent antigenic presentation of encoded antigens. We have tested a DNA vaccine specific for human immunodeficiency virus type 1 (HIV-1) by the injection of animals with expression plasmids encoding the HIV-1 envelope protein and the Rev regulatory protein. Injection of both plasmids into mice, rabbits, or macaques was found to induce high levels of specific antibodies capable of efficiently inhibiting both HIV-1 infection and envelope-mediated cell fusion. A readily detectable delayed-type hypersensitivity (DTH) response was demonstrable in injected mice and lymphocytes derived from these proliferated in response to an HIV-1 envelope V3 loop-specific peptide. Interestingly, the injected mice or macaques also developed a strong cytotoxic T lymphocyte (**CTL**) **response** against target cells pulsed with the V3 peptide. Taken together, these data demonstrate that injection of HIV-1 gene expression plasmids can induce potent humoral and cell-mediated immune responses and suggest that DNA vaccines may prove to be significantly beneficial as a means of immunizing against HIV-1.

L17 ANSWER 7 OF 7 MEDLINE on STN DUPLICATE 5
94309169. PubMed ID: 8035504. **Direct injection** of a recombinant retroviral vector induces human immunodeficiency virus-specific immune responses in mice and nonhuman primates. Irwin M J; Laube L S; Lee V; Austin M; Chada S; Anderson C G; Townsend K; Jolly D J; Warner J F. (Department of Immunobiology, Viagene, Inc., San Diego, California 92121.) Journal of virology, (1994 Aug) 68 (8) 5036-44. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB The cytotoxic T-lymphocyte (**CTL**) **response** plays an important role in controlling the severity and duration of viral infections. Immunization by direct in vivo administration of retroviral vector particles represents an efficient means of introducing and expressing genes and, subsequently, the proteins they encode in vivo in mammalian cells. In this manner foreign proteins can be provided to the endogenous, class I major histocompatibility complex antigen presentation pathway leading to CTL activation. A nonreplicating recombinant retroviral vector, encoding the human immunodeficiency virus type 1 (HIV-1) IIIB envelope and rev proteins, has been developed and examined for stimulation of immune responses in mouse, rhesus macaque, and baboon models. Animals were immunized by direct intramuscular injection of the retroviral vector particles. Vector-immunized mice, macaques, and baboons generated long-lived CD8+, major histocompatibility complex-restricted **CTL responses** that were HIV-1 protein specific. The **CTL responses** were found to be dependent on the ability of the retroviral vector to transduce cells. The vector also elicited

HIV-1 envelope-specific antibody responses in mice and baboons. These studies demonstrate the ability of a retroviral vector encoding HIV-1 proteins to stimulate cellular and humoral immune responses and suggest that retrovector immunization may provide an effective means of inducing or augmenting **CTL responses** in HIV-1-infected individuals.

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     (FILE 'HOME' ENTERED AT 14:05:12 ON 12 MAY 2004)

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 14:05:25 ON
     12 MAY 2004
L1             0 S FOLICLE INJECTION
L2        354385 S LYMPH NODE
L3         20700 S L2 AND INJECTION
L4           192 S L3 AND CTL RESPONSE
L5            11 S L4 AND DIRECTLY
L6             3 DUP REMOVE L5 (8 DUPLICATES REMOVED)
L7           101 S L2 AND DIRECT INJECTION
L8            10 S L7 AND LYMPH VESSEL
L9             9 DUP REMOVE L8 (1 DUPLICATE REMOVED)
L10            0 S L7 AND CTL RESPONSE
L11           27 S L7 AND TUMOR
L12           13 DUP REMOVE L11 (14 DUPLICATES REMOVED)
L13        14984 S CTL RESPONSE
L14           27 S L13 AND DIRECT INJECTION
L15            0 S L14 AND LYMPH NODE
L16            0 S L14 AND LYMPH VESSEL
L17            7 DUP REMOVE L14 (20 DUPLICATES REMOVED)

=> dup remove l4
PROCESSING COMPLETED FOR L4
L18           64 DUP REMOVE L4 (128 DUPLICATES REMOVED)

=> s l18 and antitumor
L19            4 L18 AND ANTITUMOR

=> dup remove l19
PROCESSING COMPLETED FOR L19
L20            4 DUP REMOVE L19 (0 DUPLICATES REMOVED)

=> d l20 1-4 cbib abs

L20  ANSWER 1 OF 4     MEDLINE on STN
2004034900.    PubMed ID: 14734732.   IL-21 induces tumor rejection by specific
     CTL and IFN-gamma-dependent CXC chemokines in syngeneic mice. Di Carlo
     Emma; Comes Alberto; Orengo Anna Maria; Rosso Ombretta; Meazza Raffaella;
     Musiani Piero; Colombo Mario P; Ferrini Silvano. (Dipartimento di
     Oncologia e Neuroscienze, Universita di Chieti, Chieti, Italy. ) Journal
     of immunology (Baltimore, Md. : 1950), (2004 Feb 1) 172 (3) 1540-7.
     Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States.
     Language: English.
AB   IL-21 is an immune-stimulatory four alpha helix cytokine produced by
     activated T cells.  To study the in vivo antitumor activities of
     IL-21, TS/A murine mammary adenocarcinoma cells were genetically modified
     to secrete IL-21 (TS/A-IL-21).  These cells developed small tumors that
     were subsequently rejected by 90% of s.c. injected syngeneic mice.  Five
     days after injection, TS/A-IL-21 tumors showed numerous
     infiltrating granulocytes, NK cells, and to a lesser extent CD8(+) T
     cells, along with the expression of TNF-alpha, IFN-gamma, and endothelial
     adhesion molecules ICAM-1 and VCAM-1.  At day 7, CD8(+) and CD4(+) T cells
     increased together with IFN-gamma, and the CXC chemokines
     IFN-gamma-inducible protein 10, monokine induced by IFN-gamma, and
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IFN-inducible T cell alpha-chemoattractant. The TS/A-IL-21 tumor displayed a disrupted vascular network with abortive sprouting and signs of endothelial cell damage. In vivo depletion experiments by specific Abs showed that rejection of TS/A-IL-21 cells required CD8(+) T lymphocytes and granulocytes. When injected in IFN-gamma-deficient mice, TS/A-IL-21 cells formed tumors that regressed in only 29% of animals, indicating a role for IFN-gamma in IL-21-mediated **antitumor** response, but also the existence of IFN-gamma-independent effects. Most immunocompetent mice rejecting TS/A-IL-21 cells developed protective immunity against TS/A-pc (75%) and against the antigenically related C26 colon carcinoma cells (61%), as indicated by rechallenge experiments. A specific **CTL response** against the gp70-env protein of an endogenous murine retrovirus coexpressed by TS/A and C26 cells was detected in mice rejecting TS/A-IL-21 cells. These data suggest that IL-21 represents a suitable adjuvant in inducing specific **CTL responses.**

L20 ANSWER 2 OF 4 MEDLINE on STN

2003544503. PubMed ID: 14607902. IL-2 intratumoral immunotherapy enhances CD8+ T cells that mediate destruction of tumor cells and tumor-associated vasculature: a novel mechanism for IL-2. Jackaman Connie; Bundell Christine S; Kinnear Beverley F; Smith Alison M; Filion Pierre; van Hagen Deborah; Robinson Bruce W S; Nelson Delia J. (School of Medicine and Pharmacology, University of Western Australia.) Journal of immunology (Baltimore, Md. : 1950), (2003 Nov 15) 171 (10) 5051-63. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Therapeutic use of IL-2 can generate **antitumor** immunity; however, a variety of different mechanisms have been reported. We injected IL-2 intratumorally (i.t.) at different stages of growth, using our unique murine model of mesothelioma (AE17; and AE17 transfected with secretory OVA (AE17-sOVA)), and systematically analyzed real-time events as they occurred in vivo. The majority of mice with small tumors when treatment commenced displayed complete tumor regression, remained tumor free for >2 mo, and survived rechallenge with AE17 tumor cells. However, mice with large tumors at the start of treatment failed to respond. Timing experiments showed that IL-2-mediated responses were dependent upon tumor size, not on the duration of disease. Although i.t. IL-2 did not alter tumor Ag presentation in draining **lymph nodes**, it did enhance a previously primed, endogenous, tumor-specific in vivo **CTL response** that coincided with regressing tumors. Both CD4(+) and CD8(+) cells were required for IL-2-mediated tumor eradication, because IL-2 therapy failed in CD4(+)-depleted, CD8(+)-depleted, and both CD4(+)- and CD8(+)-depleted C57BL/6J animals. Tumor-infiltrating CD8(+) T cells, but not CD4(+) T cells, increased in association with a marked reduction in tumor-associated vascularity. Destruction of blood vessels required CD8(+) T cells, because this did not occur in nude mice or in CD8(+)-depleted C57BL/6J mice. These results show that repeated doses of i.t. (but not systemic) IL-2 mediates tumor regression via an enhanced endogenous tumor-specific **CTL response** concomitant with reduced vasculature, thereby demonstrating a novel mechanism for IL-2 activity.

L20 ANSWER 3 OF 4 MEDLINE on STN

2000171509. PubMed ID: 10706699. CD8+ T cell-dependent elimination of dendritic cells in vivo limits the induction of **antitumor** immunity. Hermans I F; Ritchie D S; Yang J; Roberts J M; Ronchese F. (Malaghan Institute of Medical Research, Wellington School of Medicine, Wellington, New Zealand.) Journal of immunology (Baltimore, Md. : 1950), (2000 Mar 15) 164 (6) 3095-101. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB The fate of dendritic cells (DC) after they have initiated a T cell immune response is still undefined. We have monitored the migration of DC labeled with a fluorescent tracer and injected s.c. into naive mice or into mice with an ongoing immune response. DC not loaded with Ag were detected in the draining **lymph node** in excess of 7

days after **injection** with maximum numbers detectable approximately 40 h after transfer. In contrast, DC that had been loaded with an MHC class I-binding peptide disappeared from the **lymph node** with kinetics that parallel the known kinetics of activation of CD8+ T cells to effector function. In the presence of high numbers of specific CTL precursors, as in TCR transgenic mice, DC numbers were significantly decreased by 72 h after **injection.** The rate of DC disappearance was extremely rapid and efficient in recently immunized mice and was slower in "memory" mice in which memory CD8+ cells needed to reacquire effector function before mediating DC elimination. We also show that CTL-mediated clearance of Ag-loaded DC has a notable effect on immune responses in vivo. Ag-specific CD8+ T cells failed to divide in response to Ag presented on a DC if the DC were targets of a pre-existing **CTL response.** The induction of **antitumor** immunity by tumor Ag-loaded DC was also impaired. Therefore, CTL-mediated clearance of Ag-loaded DC may serve as a negative feedback mechanism to limit the activity of DC within the **lymph node.**

L20 ANSWER 4 OF 4 MEDLINE on STN

2000005758. PubMed ID: 10537366. Antibodies to vascular endothelial growth factor enhance the efficacy of cancer immunotherapy by improving endogenous dendritic cell function. Gabrilovich D I; Ishida T; Nadaf S; Ohm J E; Carbone D P. (Department of Medicine and The Vanderbilt Cancer Center, Vanderbilt University School of Medicine, Nashville, Tennessee 37232-6838, USA.. dgabril@luc.edu) . Clinical cancer research : an official journal of the American Association for Cancer Research, (1999 Oct) 5 (10) 2963-70. Journal code: 9502500. ISSN: 1078-0432. Pub. country: United States. Language: English.

AB Inadequate function of dendritic cells (DCs) in tumor-bearing hosts is one mechanism of tumor escape from immune system control and may compromise the efficacy of cancer immunotherapy. Vascular endothelial growth factor (VEGF), produced by most tumors, not only plays an important role in tumor angiogenesis but also can inhibit the maturation of DCs from hematopoietic progenitors. Here, we investigate a novel combination of antiangiogenic and immunotherapy based on this dual role of VEGF. Two s.c. mouse tumor models were used: D459 cells, expressing mutant human p53; and MethA sarcoma with point mutations in the endogenous murine p53 gene. Therapy with anti-mouse VEGF antibody (10 microg i.p. twice a week over 4 weeks) was initiated when tumors became palpable. Treatment of established tumors with anti-VEGF antibody alone did not affect the rate of tumor growth. However, anti-VEGF antibody significantly improved the number and function of **lymph node** and spleen DCs in these tumor-bearing animals. To investigate the possible effects of this antibody on the immunotherapy of established tumors, tumor-bearing mice were immunized with DCs pulsed with the corresponding mutation-specific p53 peptides, together with **injections** of anti-VEGF antibody. Therapy with peptide-pulsed DCs alone resulted in considerable slowing of tumor growth but only during the period of treatment, and tumor growth resumed after the end of the therapy. Combined treatment with peptide-pulsed DCs and anti-VEGF antibody resulted in a prolonged and much more pronounced **antitumor** effect. This effect was associated with the induction of significant anti-p53 **CTL responses** only in this group of mice. These data suggest that inhibition of VEGF may be a valuable adjuvant in the immunotherapy of cancer.

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(FILE 'HOME' ENTERED AT 14:05:12 ON 12 MAY 2004)

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 14:05:25 ON 12 MAY 2004

L1 0 S FOLICLE INJECTION
L2 354385 S LYMPH NODE
L3 20700 S L2 AND INJECTION

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L4          192 S L3 AND CTL RESPONSE
L5           11 S L4 AND DIRECTLY
L6            3 DUP REMOVE L5 (8 DUPLICATES REMOVED)
L7          101 S L2 AND DIRECT INJECTION
L8           10 S L7 AND LYMPH VESSEL
L9            9 DUP REMOVE L8 (1 DUPLICATE REMOVED)
L10           0 S L7 AND CTL RESPONSE
L11          27 S L7 AND TUMOR
L12          13 DUP REMOVE L11 (14 DUPLICATES REMOVED)
L13       14984 S CTL RESPONSE
L14          27 S L13 AND DIRECT INJECTION
L15           0 S L14 AND LYMPH NODE
L16           0 S L14 AND LYMPH VESSEL
L17           7 DUP REMOVE L14 (20 DUPLICATES REMOVED)
L18          64 DUP REMOVE L4 (128 DUPLICATES REMOVED)
L19           4 S L18 AND ANTITUMOR
L20           4 DUP REMOVE L19 (0 DUPLICATES REMOVED)

=> s l2 and direct injection
L21         101 L2 AND DIRECT INJECTION

=> dup remove l21
PROCESSING COMPLETED FOR L21
L22          50 DUP REMOVE L21 (51 DUPLICATES REMOVED)

=> d l22 1-50 cbib abs

L22  ANSWER 1 OF 50  EMBASE  COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN                                                DUPLICATE 1
2004113784  EMBASE  Optimised nuclear medicine method for tumour marking and
     sentinel node detection in occult primary breast lesions. De Cicco C.;
     Trifiro G.; Intra M.; Marotta G.; Ciprian A.; Frasson A.; Prisco G.; Luini
     A.; Viale G.; Paganelli G.. C. De Cicco, Division of Nuclear Medicine,
     European Institute of Oncology, University of Milan, Via Ripamonti,
     435-20141 Milan, Italy. concetta.de-cicco@ieo.it. European Journal of
     Nuclear Medicine and Molecular Imaging  31/3 (349-354)  2004.
     Refs: 17.
     ISSN: 1619-7070. CODEN: EJNMA6. Pub. Country: Germany. Language: English.
     Summary Language: English.
AB   The aim of this study was to evaluate the feasibility of sentinel node
     (SN) biopsy in occult breast lesions with different radiopharmaceuticals
     and to establish the optimal lymphoscintigraphic method to detect both
     occult lesions and SNs (SNOLL: sentinel node and occult lesion
     localisation). Two hundred and twenty-seven consecutive patients suspected
     to have clinically occult breast carcinoma were enrolled in the study. In
     addition to the radioguided occult lesion localisation (ROLL) procedure,
     using macroaggregates of technetium-99m labelled human serum albumin (MAA)
     injected directly into the lesion, lymphoscintigraphy was performed with
     nanocolloids (NC) injected in a peritumoral (group I) or a subdermal site
     (group II). In group III, a sole injection of NC was done into the lesion
     in order to perform both ROLL and SNOLL. Overall, axillary SNs were
     identified in 205 of the 227 patients (90.3%). In 12/62 (19.4%) patients
     of group I and 9/79 (11.4%) patients of group III, radioactive nodes were
     not visualised, whereas SNs were successfully localised in 85 of 86
     patients of group II (P<0.001). Pathological findings revealed breast
     carcinoma in 148/227 patients (65.2%) and benign lesions in 79 (34.8%). A
     total of 131 axillary SNs were removed in 118 patients with breast
     carcinoma; intraoperative examination of the SNs revealed metastatic
     involvement in 16 out of 96 cases of invasive c arcinoma (16.7%). It is
     concluded that the combination of the ROLL procedure with direct
     injection of MAA into the lesion and lymphoscintigraphy performed
     with subdermal injection of radiocolloids represents the method of choice
     for accurate localisation of both non-palpable lesions and SNs.

L22  ANSWER 2 OF 50  CAPLUS  COPYRIGHT 2004 ACS on STN
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2002:276188 Document No. 136:289366 Use of VEGF as a lymphangiogenic agents to treat lymphatic disorders. Gravereaux, Edwin C.; Silver, Marcy; Isner, Jeffrey M.; Yoon, Young-Sup (St. Elizabeth's Medical Center of Boston, Inc., USA). PCT Int. Appl. WO 2002029087 A2 20020411, 77 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US30904 20011002. PRIORITY: US 2000-PV237171 20001002.

AB The present invention provides methods for promoting the growth of new lymph vessels (lymphangiogenesis). Generally, such methods include administering at least one vascular endothelian factor (VEGF) such as VEGF-2. In one embodiment, therapeutic methods for treating lymphedema and related disorders in a human patient are disclosed. The VEGF can be provided by any suitable means including **direct injection** of a nucleic acid encoding same or an active fragment thereof. Also provided are pharmaceutical products for promoting lymphangiogenesis as well as a test system for screening compds. capable of inducing new lymph vessel growth. Addnl., the rabbit VEGFR-3 cDNA and protein are both claimed.

L22 ANSWER 3 OF 50 CAPLUS COPYRIGHT 2004 ACS on STN

2002:794299 Document No. 137:320695 Use of VEGFs as lymphangiogenic agents to treat lymphatic disorders. Gravereaux, Edwin C.; Silver, Marcy; Yoon, Young-sup; Isner, Jeffrey M.; Isner, Linda (St. Elizabeth's Medical Center of Boston, Inc., USA). U.S. Pat. Appl. Publ. US 2002151489 A1 20021017, 54 pp., Cont.-in-part of U. S. Provisional Ser. No. 237,171. (English). CODEN: USXXCO. APPLICATION: US 2001-970088 20011002. PRIORITY: US 2000-PV237171 20001002.

AB The present invention provides methods for promoting the growth of new lymph vessels (lymphangiogenesis). Generally, such methods include administering at least one vascular endothelian factor (VEGF) such as VEGF-2. In one embodiment, therapeutic methods for treating lymphedema and related disorders in a human patient are disclosed. The VEGF can be provided by any suitable means including **direct injection** of a nucleic acid encoding same or an active fragment thereof. Also provided are pharmaceutical products for promoting lymphangiogenesis as well as a test system for screening compds. capable of inducing new lymph vessel growth. Also provided are pharmaceutical products for promoting lymphangiogenesis as well as a test system for screening compds. capable of inducing new lymph vessel growth. Addnl., fragments of the rabbit VEGFR-3 cDNA and protein are both claimed.

L22 ANSWER 4 OF 50 MEDLINE on STN DUPLICATE 2

2002451907. PubMed ID: 12209648. Lack of antigen-specific immune responses in anti-IL-7 receptor alpha chain antibody-treated Peyer's patch-null mice following intestinal immunization with microencapsulated antigen. Kunisawa Jun; Takahashi Ichiro; Okudaira Akiko; Hiroi Takachika; Katayama Kazufumi; Ariyama Teruko; Tsutsumi Yasuo; Nakagawa Shinsaku; Kiyono Hiroshi; Mayumi Tadanori. (Department of Mucosal Immunology, Research Institute for Microbial Diseases, Osaka University, Osaka, Japan.) European journal of immunology, (2002 Aug) 32 (8) 2347-55. Journal code: 1273201. ISSN: 0014-2980. Pub. country: Germany: Germany, Federal Republic of. Language: English.

AB Peyer's patches (PP) represent a well-characterized inductive site in gut-associated lymphoid tissue that actively acquires antigens from the intestinal lumen. It was reported that organized PP are not required for antigen-specific IgA responses induced by oral immunization with soluble antigen mixed with the mucosal adjuvant, cholera toxin. However, the role of PP in the induction of mucosal and systemic immune responses remains to be clarified in the case of particulate antigen. Here, we created PP-null

mice by treating them with monoclonal anti-IL-7 receptor alpha chain (IL-7 R alpha) antibody during gestation and then immunized with antigen-encapsulated poly-lactic acid (PLA) microspheres. Brisk OVA-specific antibody responses were noted in serum and fecal extracts of normal mice following direct intestinal immunization with OVA in PBS (OVA-PBS) as well as in PLA-microspheres (OVA-MS). Antibody production was similarly elevated in PP-null mice immunized with OVA-PBS via **direct injection** into the intestinal tract. In contrast, OVA-specific antibody responses were dramatically decreased in both serum and fecal extracts collected from PP-null mice immunized intestinally with OVA-MS. These results were further supported by the number of OVA-specific antibody-forming cells detected in the spleen and intestinal lamina propria. PP deficiency also resulted in the reduction in OVA-specific Th1/Th2 cell responses in the spleen and mesenteric **lymph nodes** of mice intestinally immunized with OVA-MS. These results suggested that organized PP do, in fact, play a crucial role in the induction of antigen-specific immune responses against ingested particulate antigen.

L22 ANSWER 5 OF 50 MEDLINE on STN DUPLICATE 3

2002383730. PubMed ID: 12133274. Oncolytic herpesvirus effectively treats murine squamous cell carcinoma and spreads by natural lymphatics to treat sites of lymphatic metastases. Wong Richard J; Joe John K; Kim Se-Heon; Shah Jatin P; Horsburgh Brian; Fong Yuman. (Head and Neck Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY 10021, USA.) Human gene therapy, (2002 Jul 1) 13 (10) 1213-23. Journal code: 9008950. ISSN: 1043-0342. Pub. country: United States. Language: English.

AB Oncolytic herpesviruses have significant antitumoral effects in animal models when delivered directly to established tumors. Lymphatic metastases are a common occurrence for many tumor types. This study investigates the potential of an attenuated, replication-competent, oncolytic herpes simplex virus (NV1023) both to treat a primary tumor by **direct injection** and to travel through the lymphatic system to treat metastatic tumor within the **lymph nodes** draining lymph from the site of primary cancer. Isosulfan blue dye was injected into murine auricles to determine normal lymphatic drainage patterns and demonstrated consistent blue staining of a group of ipsilateral cervical **lymph nodes.** Auricular injections of NV1023 resulted in viral transit to these **lymph nodes** as measured by 5-bromo-4-chloro-3-indolyl-beta-D-galactopyranoside histochemistry and viral plaque assay. An oncolytic herpesvirus (NV1066) expressing green fluorescent protein also demonstrated viral transit from the auricle to the cervical **lymph nodes** on fluorescence microscopy. Using the SCC VII cell line, a novel murine model of auricular squamous cell carcinoma was developed with an approximately 20% incidence of cervical **lymph node** metastases. Delivery of NV1023 or NV1066 to the surgical beds after excision of auricular SCC VII tumors resulted in successful viral infection of metastatic SCC VII cells within the cervical **lymph nodes.** After a 7-week follow-up, significantly enhanced locoregional control ($p < 0.05$, Fisher exact test) and disease-free survival ($p < 0.05$, log rank test) were evident with NV1023 treatment. This study demonstrates that the delivery of an oncolytic herpesvirus to a primary tumor site after surgical excision may have a significant impact on reducing both primary site recurrence and regional nodal metastases.

L22 ANSWER 6 OF 50 MEDLINE on STN DUPLICATE 4

2002182449. PubMed ID: 11916241. Suppression of murine mammary carcinoma growth and metastasis by HSVtk/GCV gene therapy using in vivo electroporation. Shibata Masa-Aki; Morimoto Junji; Otsuki Yoshinori. (Department of Anatomy and Biology, Osaka Medical College, Takatsuki, Japan.) Cancer gene therapy, (2002 Jan) 9 (1) 16-27. Journal code: 9432230. ISSN: 0929-1903. Pub. country: England: United Kingdom. Language: English.

AB The effectiveness of electroporation as a means of gene transfection, both in vitro and in vivo, was tested using the herpes simplex virus 1 thymidine kinase (HSVtk) gene in combination with ganciclovir (GCV) administration as therapy against murine mammary cancer. Approximately 80% of BJMC3879 metastatic mammary carcinoma cells, derived from MMTV-infected BALB/c mice, died as a result of HSVtk/GCV treatment 72 hours after the transfection; decreased DNA synthesis was also seen. Mammary tumors induced by inoculation of syngeneic mice with BJMC3879 cells were subsequently treated by **direct injection** of vector containing HSVtk (pHSVtk) alone, empty vector or saline alone twice a week. After each injection, the tumors were subjected to in vivo electroporation. Mice treated with pHSVtk or saline were intraperitoneally injected with GCV at 40 mg/kg five times a week. Significantly reduced tumor volumes were observed for the pHSVtk+GCV group in experimental week 2 and thereafter throughout the 2-month study. DNA synthesis was significantly decreased as well in the pHSVtk+GCV group compared with all other groups. Furthermore, metastasis to **lymph nodes** and lungs was significantly suppressed by HSVtk/GCV treatment. Expression of HSVtk in the tumors was confirmed by RT-PCR. Macrophage accumulations were frequently observed in the peripheries of necrotic regions in HSVtk/GCV-treated tumors, where levels of apoptosis were significantly higher than those observed in other groups. We therefore conclude that in vivo electroporation can result in efficient gene transfer and that the HSVtk/GCV prodrug system strongly suppresses tumor growth and metastases in this model.

L22 ANSWER 7 OF 50 MEDLINE on STN
2001653877. PubMed ID: 11706493. [Lymphadenography--pioneering work of Sven Bruun and Arnfinn Engeset]. Lymfadenografi--pionerarbeid av Sven Bruun og Arnfinn Engeset. Kolbenstvedt A. (Radiologisk avdeling Rikshospitalet 0027 Oslo.) Tidsskrift for den Norske laegeforening, (2001 Oct 10) 121 (24) 2836-7. Journal code: 0413423. ISSN: 0029-2001. Pub. country: Norway. Language: Norwegian.

AB Lymphadenography is a method for direct radiologic visualization of **lymph nodes** following injection of fat soluble contrast medium. Sven Bruun and Arnfinn Engeset at Rogaland Hospital developed this method in 1952 and published preliminary results in 1956. They have been somewhat overshadowed by the English surgeon John B. Kinmonth who published his method on lymphangiography in 1954. Kinmonth succeeded in visualizing the peripheral lymph vessels by **direct injection** of water soluble contrast medium. By this technique it was not feasible to depict **lymph nodes** above the knee because of diffusion of medium to surrounding tissues. Lymphography is a technique that visualizes both lymph vessels and **lymph nodes.** This method is based on a combination of the two above-mentioned methods with injection of fat soluble contrast medium into peripheral lymph vessels. Lymphography was a very important examination which was used all over the world in the 1960s and 1970s. It has now been replaced by other examinations.

L22 ANSWER 8 OF 50 MEDLINE on STN DUPLICATE 5
2002007199. PubMed ID: 11248073. Intralymphatic immunization enhances DNA vaccination. Maloy K J; Erdmann I; Basch V; Sierro S; Kramps T A; Zinkernagel R M; Oehen S; Kundig T M. (Department of Dermatology, and Institute of Experimental Immunology, Universitatsspital Zurich, Schmelzbergstrasse 12, CH-8091 Zurich, Switzerland.. kevin.maloy@path.ox.ac.uk) . Proceedings of the National Academy of Sciences of the United States of America, (2001 Mar 13) 98 (6) 3299-303. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB Although DNA vaccines have been shown to elicit potent immune responses in animal models, initial clinical trials in humans have been disappointing, highlighting a need to optimize their immunogenicity. Naked DNA vaccines are usually administered either i.m. or intradermally. The current study shows that immunization with naked DNA by **direct**

injection into a peripheral **lymph node** enhances immunogenicity by 100- to 1,000-fold, inducing strong and biologically relevant CD8(+) cytotoxic T lymphocyte responses. Because injection directly into a **lymph node** is a rapid and easy procedure in humans, these results have important clinical implications for DNA vaccination.

L22 ANSWER 9 OF 50 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
2001:504220 The Genuine Article (R) Number: 443QA. Safety and pharmacokinetics of naked plasmid DNA in the skin: Studies on dissemination and ectopic expression. Hengge U R (Reprint); Dexling B; Mirmohammadsadegh A. Univ Essen Gesamthsch, Dept Dermatol Venerol & Allergol, Hufelandstr 55, D-45122 Essen, Germany (Reprint); Univ Essen Gesamthsch, Dept Dermatol Venerol & Allergol, D-45122 Essen, Germany. JOURNAL OF INVESTIGATIVE DERMATOLOGY (JUN 2001) Vol. 116, No. 6, pp. 979-982. Publisher: BLACKWELL SCIENCE INC. 350 MAIN ST, MALDEN, MA 02148 USA. ISSN: 0022-202X. Pub. country: Germany. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Gene therapy using naked DNA injected into muscle and skin is increasingly being used for vaccination and treatment purposes. Favorably, naked plasmid DNA does not exhibit the various limitations inherent to viral vectors, such as the elicitation of adverse immune responses and the risk of insertional mutagenesis. In order to assess the distribution and safety of naked plasmid DNA in a relevant animal model, we analyzed if intracutaneously injected plasmid DNA was transported to other organs and if ectopic expression occurred. When a "superdose" of a marker plasmid was injected intradermally, most organs were found transiently to contain the plasmid DNA for several days, whereas integration into the host genome was not detected. With the exception of ovary, however, mRNA expression only occurred in the skin, regional **lymph nodes**, and muscular tissues. From a safety standpoint, skin gene therapy with naked plasmid DNA can be considered safe due to the rapid biodegradation of plasmid DNA and the exclusive and transient expression of foreign genes in tissues known to take up DNA.

L22 ANSWER 10 OF 50 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
2001:459852 The Genuine Article (R) Number: 437LL. Rapid and wide-reaching delivery of HIV-1 env DNA vaccine by intranasal administration. Tadokoro K; Koizumi Y; Miyagi Y; Kojima Y; Kawamoto S; Hamajima K; Okuda K (Reprint); Tanaka S; Onari K; Wahren B; Aoki I; Okuda K. Yokohama City Univ, Sch Med, Dept Bacteriol, Kanazawa Ku, 3-9 Fukuura, Yokohama, Kanagawa 2360004, Japan (Reprint); Yokohama City Univ, Sch Med, Dept Bacteriol, Kanazawa Ku, Yokohama, Kanagawa 2360004, Japan; Yokohama City Univ, Sch Med, Dept Internal Med, Yokohama, Kanagawa 2360004, Japan; Yokohama City Univ, Sch Med, Dept Pathol, Yokohama, Kanagawa 2360004, Japan; Tokyo Dent Coll, Dept Bacteriol, Mihama Ku, Masago, Japan; Yokohama Minami Kyosai Hosp, Dept Orthoped Surg, Yokohama, Kanagawa, Japan; Karolinska Inst, Swedish Inst Infect Dis Control, Stockholm, Sweden. VIRAL IMMUNOLOGY (5 MAY 2001) Vol. 14, No. 2, pp. 159-167. Publisher: MARY ANN LIEBERT INC PUBL. 2 MADISON AVENUE, LARCHMONT, NY 10538 USA. ISSN: 0882-8245. Pub. country: Japan; Sweden. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Although the potential of DNA vaccination is now beginning to be greatly appreciated, no detailed study of its localization in tissue or its expression kinetics has been reported. In this study, we investigated these issues using HIV-1 DNA plasmids administered either intranasally or intramuscularly, Fluorescence in situ hybridization (FISH) revealed that the human immunodeficiency virus (HIV) plasmids administered intranasally localized in the alveoli, lung, liver, spleen, regional **lymph nodes**, kidney, fetus, and esophagus, These HIV plasmids were detected 2 to 4 weeks after administration. We detected messenger RNA production of HIV env gene in the lung, liver and spleen, and human immunodeficiency virus type 1 (HIV-1)-specific proteins were detectable in the lung, These observations may provide important information for understanding the mechanisms of strong immune activation induced by DNA

vaccination via the intranasal route. This technology of DNA administration suggests possible practical applications for vaccination and probably for gene therapy.

L22 ANSWER 11 OF 50 MEDLINE on STN DUPLICATE 6

1999398752. PubMed ID: 10467363. Distribution of retroviral vectors and vector producer cells using two routes of administration in rats. Kaloss M; Linscott M; Wey C; Lu P; Long Z; McGarrity G J; Otto E; Lyons R M. (Genetic Therapy, Inc, 938 Clopper Road, Gaithersburg, MD 20878, USA.) Gene therapy, (1999 Aug) 6 (8) 1389-96. Journal code: 9421525. ISSN: 0969-7128. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The clinical use of retroviral vector producer cells (VPCs) to deliver retroviral vectors efficiently to target cells has been investigated as a method to increase efficiency of gene delivery, presumably as a result of continued vector production in vivo. Studies were conducted in rats to evaluate the distribution of vector to distal organs and tissues as measured by transduction. Rats were treated with two doses of VPCs using two routes of administration: (1) subcutaneous injection, chosen to maximize both the dose and exposure of animals, thereby enabling identification of potential target organs under worst-case conditions; and (2) **direct injection** into brain parenchyma, chosen to mimic the intended clinical route of administration and provide an estimate of risk to patients receiving this therapy. Twelve organs or tissues were collected 7 days after administration of VPCs and analyzed by PCR for the presence of vector and vector producer cell sequences. Vector was detected most frequently at the site of injection by either route of administration. Less frequently, vector was detected in draining **lymph nodes** at the higher dose only using either route of injection. Single specimens of lung and contralateral skin were positive for vector following subcutaneous administration only. Vector was detected in gonadal tissue from a single low-dose male following subcutaneous administration, but this finding was not reproduced in any high-dose male or any males injected intracerebrally. In contrast, VPCs were detected only at the site of administration. The frequency of detection of VPCs 7 days after administration was higher when rats were injected by the intracerebral route. Based on these studies, gene transfer to distal organs or gonadal tissue following intracerebral administration of VPCs is not considered to be a risk to patients undergoing retroviral vector gene therapy for the treatment of brain cancer (glioblastoma multiforme; GBM).

L22 ANSWER 12 OF 50 EMBASE on STN

2000093020 EMBASE Lymphatic drainage of the heart and lungs in the pig: A preliminary study. Riquet M.; Hubsch J.P.; Chehab A.; Briere J.; Colomer S.; Hidden G.. Prof. M. Riquet, Laennec Hospital, Service de Chirurgie Thoracique, 42 rue de Sevres, 75007 Paris, France. riquet@lnc.ap-hop-paris.fr. European Journal of Lymphology and Related Problems 7/27 (80-84) 1999.
Refs: 17.
ISSN: 0778-5569. CODEN: EJLPE. Pub. Country: Belgium. Language: English. Summary Language: English.

AB In anatomy and physiology the pig is remarkably like man and is therefore considered as Potential Organ Donor. It was then particularly interesting to reconsider the lymphatic drainage of both its heart and lungs (H.L)Fifteen dead pigs were studied. The technique comprised removal of the sternocostal shield and injection into the myocardium and/or beneath the visceral pleura of a colored mass that was supplemented by **direct injection** of the nodes revealed in that manner.
First colored nodes were tracheobronchial located-under the tracheal carina (ITBN), above the left (LSBN) and right (RSBN) main bronchus, above the right upper lobe tracheal bronchus (TBN) - and located at the lower level of the cervical trachea (CMN). There was no other pretracheal neither pulmonary LN contrary to human. The lymphatic vessels (LV) of the heart connected with the LSBN, rarely with the CMN. The LV issuing from :

the ITBN connected with both the RSBN and LSBN and also with retrotracheal lymphcenter nodes (RTN); the RSBN connected with RTN, CMN or drained into the right jugulo subclavian venous confluent; The LSBN connected at times with RSBN and some lateroesophageal nodes, but generally drained into the left jugulosubclavian venous confluent, the arch of the thoracic duct (TD) and directly into the TD in the middle mediastinum, also an important lymph pathway in human. Lymphatics of the H.L. in pigs display anatomical patterns rarely observed in man but phylogeneticly explaining diseases as 'skipping' node metastases in lung cancer and chylothorax after heart and lungs surgery. In anatomy and physiology, the pig is remarkably like man. In 1966, Glauser underlined the advantages of Piglets as Experimental Animals in Pediatric Resarch : laboratory data comparing the newborn infant with the newborn piglet disclosed a striking similarity in the results reported for respiratory system. In adult research the pig's size proved to be a problem that was solved by breeding miniature pigs. Porcine coronary arteries have almost the same pattern as the human being and investigators have found the pig particularly valuable for the study of coronary arteriosclerosis. The similitude between the 2 species are so great and the differences so little that since recently pig is considered as a potential organ donor and most of its organs are thought suitable for xenotransplantation. In view of contributing to such major topics, it seemed particularly interesting to reconsider the lymphatic drainage of both heart and lungs in this species so closely related to human.

L22 ANSWER 13 OF 50 MEDLINE on STN DUPLICATE 7

1999068049. PubMed ID: 9851063. Three-dimensional and ultrastructural aspects of the lymphatic vascularization of the vermiform appendix. Azzali G. (Institute of Human Anatomy, Faculty of Medicine, University of Parma, Italy.. anatnor@ipruniv.cce.unipr.it) . Journal of submicroscopic cytology and pathology, (1998 Oct) 30 (4) 545-53. Journal code: 8804312. ISSN: 1122-9497. Pub. country: Italy. Language: English.

AB The aim of the study is to reveal the three-dimensional distribution and ultrastructure of the peripheral absorbing lymphatic vessels of the vermiform appendix, since the gut-associated lymphoid tissue is necessary to the immune responses to the enteric antigens. Corrosion casts showed the beginning of the lymphatic vascularization at the tunica mucosa, which lacks intestinal villi, through a tight, delicate lymphatic network. This network drains the lymph by peculiar straight vessels, distributed in the mucosal beams that separate the adjacent follicle domes, in the fine network of the upper portion of the lymphatic basket, surrounding the lateral walls of the basal and medium portions of each lymphoid follicle. This network, which is made of large caliber vessels that are not dilated like sinuses, continues through small vessels into the large dome-like vessels of the submucosa, which in turn by way of the lymphatic vessels of the muscular tunica, drain into the subserous precollector valved lymphatic vessels that flow into the pre-**lymph node** collectors. We underlined that the particular fluidity of Neoprene latex and the **direct injection** method, when compared with other substances and injection methods, provided us with exceptionally clear and precise three-dimensional plastic images of the absorbing lymphatic vessels. Moreover, these images extraordinarily illustrated the preservation of the absorbing lymphatic spatial relationships with blood vessels. Ultrastructural features and three-dimensional models of ultrathin serial sections of the absorbing peripheral lymphatic vessels showed a continuous endothelial wall lacking basal lamina, as well as open junctions between adjacent cells. Moreover, we observed the presence of numerous lymphocytes, together with intense transendothelial migratory activity that occurs through intraendothelial channel formations, dynamic entities, at absorbing lymphatic vessels of the peri-interfollicular lymphoid tissue. Also, we saw that the germinal center, as well as the lymphoid follicle dome, lacked lymphatic absorbing vessels. In addition, many postcapillary high endothelial venules (HEV) were observed with lymphocyte migration into the extravasal compartment. Furthermore, we maintain that the absorbing peripheral lymphatic vessels (ALPA) of the tunica mucosa play an important role in liquid drainage. For the

peri-interfollicular vessels, we hypothesize a potential migratory and a reserve capacity for lymphocytes, as well as a conduction activity for the muscular tunica and submucosa vessels.

L22 ANSWER 14 OF 50 CAPLUS COPYRIGHT 2004 ACS on STN
1997:464640 Document No. 127:175168 Deletion of alloantigen-reactive thymocytes as a mechanism of adult tolerance induction following intrathymic antigen administration. Jones, Nick D.; Fluck, Nick C.; Roelen, Dave L.; Mellor, Andrew L.; Morris, Peter J.; Wood, Kathryn J. (John Radcliffe Hospital, University Oxford, Oxford, OX3-9DU, UK). European Journal of Immunology, 27(7), 1591-1600 (English) 1997. CODEN: EJIMAF. ISSN: 0014-2980. Publisher: Wiley-VCH.

AB **Direct injection** of foreign antigen into the adult thymus is a potent route of antigen delivery for the induction of tolerance in vivo. It was demonstrated that tolerance to C57BL/10 (H2b/BL10) alloantigens can be induced in CBA/Ca (H2k/CBA) mice by intrathymic (IT) administration of BL10 spleen leukocytes coincident with transient peripheral immunomodulation of CD4+ T cells using a depleting anti-CD4 monoclonal antibody. T cell receptor (TCR) transgenic mice (BM3.6; H2k) expressing a CD8-independent TCR specific for H2Kb were used as recipients to facilitate investigation of the mechanisms responsible for tolerance induction by allowing visualization of events in the thymus following IT injection. IT administration of 5 + 107 BL10 spleen leukocytes and concomitant transient peripheral T cell depletion in BM3.6 mice resulted in a substantial H2Kb-specific deletion of transgenic-TCR+ (tg-TCR) thymocytes which was dependent on the level of tg-TCR expression. IT deletion and the failure to export CD8+ T cells to the peripheral lymphoid organs correlated with the induction of tolerance to H2Kb, TCR transgenic mice that had received IT injection of BL10 splenocytes and peripheral T cell depletion accepted a H2Kb+ cardiac allograft indefinitely. Anal. of tolerant BM3.6 mice revealed that there were low nos. of CD8+ T cells in the periphery giving rise to a substantially reduced reactivity in vitro despite the fact that no donor cells or IT deletion were observed in the thymi of the majority of tolerant mice. These results demonstrate for the first time that IT injection of foreign alloantigen into an adult thymus results in the deletion of thymocytes expressing a TCR specific for the injected alloantigen and suggest that this is an important mechanism of tolerance induction following IT injection of alloantigen in vivo. Anal. of tolerant TCR-transgenic mice suggests that IT deletion is not required for the maintenance of tolerance, and that peripheral mechanisms enforce continued hyporesponsiveness to H2Kb following transplantation.

L22 ANSWER 15 OF 50 MEDLINE on STN DUPLICATE 8
1998033894. PubMed ID: 9367025. Cytokines as an adjuvant to tumor vaccines: efficacy of local methods of delivery. Kurane S; Arca M T; Aruga A; Krinock R A; Krauss J C; Chang A E. (Division of Surgical Oncology, University of Michigan, Ann Arbor, USA.) Annals of surgical oncology : official journal of the Society of Surgical Oncology, (1997 Oct-Nov) 4 (7) 579-85. Journal code: 9420840. ISSN: 1068-9265. Pub. country: United States. Language: English.

AB BACKGROUND: We examined alternative methods of delivering cytokines as an adjunct for priming **lymph node** (LN) cells draining sites of vaccine inoculation for the purpose of generating immune cells for adoptive immunotherapy. METHODS: Using syngeneic murine tumors we examined the ability of IL-2, IL-4, or GM-CSF delivered locally to a site of tumor inoculum to induce antitumor reactive draining LN cells. Mice were inoculated subcutaneously with tumor cells transduced to secrete cytokine; tumor cells admixed with fibroblasts transduced to secrete cytokine; or intralesional inoculation of cytokine in established tumor to induce sensitized LN cells capable of mediating tumor regression in adoptive transfer. RESULTS: Both IL-4 and GM-CSF cytokines were effective in enhancing the antitumor reactivity of vaccine-primed LN cells compared to IL-2, which was ineffective. The local delivery of GM-CSF by autocrine or paracrine secretion of genetically engineered cells, as well as direct

intratumoral delivery was capable of upregulating LN sensitization compared to systemic administration, which did not. CONCLUSIONS: The local delivery of GM-CSF as an adjuvant for tumor vaccination can be accomplished by various methods, including **direct injection**, which avoids the need for gene transfer.

L22 ANSWER 16 OF 50 MEDLINE on STN DUPLICATE 9

97413203. PubMed ID: 9267846. Use of the dog model for Duchenne muscular dystrophy in gene therapy trials. Howell J M; Fletcher S; Kakulas B A; O'Hara M; Lochmuller H; Karpati G. (School of Veterinary Studies, Murdoch University, Perth, Australia.) Neuromuscular disorders : NMD, (1997 Jul) 7 (5) 325-8. Journal code: 9111470. ISSN: 0960-8966. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Golden retriever muscular dystrophy (GRMD) is an excellent model for the study of the efficacy of gene therapy in dystrophin deficient myopathies for there are many similarities between affected dogs and Duchenne muscular dystrophy (DMD) in boys. GRMD is not caused by deletion mutation but results from a point mutation in the consensus splice acceptor in intron 6 of the canine dystrophin gene. As a result exon 7 is skipped during processing of the GRMD dystrophin messenger RNA. We have developed a rapid test which makes direct use of exon 7 specific genomic PCR products. We have undertaken preliminary experiments on gene therapy using the mini-gene and the full length gene alone and in combination with lipofectin and/or the bacterial beta-galactosidase reporter gene Lac Z. Following **direct injection** of the Lac Z plasmid, either alone or with lipofectin, about 50% of the sites showed expression when biopsied some 14 days later. The beta-galactosidase activity was present in muscle and granulation tissue but was never abundant. Pups injected intraperitoneally with Lac Z were found to have positive material in their mesenteric **lymph nodes**, liver and spleen. Those injected with Lac Z and lipofectin also had positive material in the diaphragm, intercostal muscles and abdominal muscles, but again only a small amount of positive material was present at any of the sites. In animals directly injected into the muscle with the dystrophin mini-gene, half had positive staining for dystrophin in biopsies taken 14 days later. Of the 6 sites in the muscles of animals given the mini-gene and lipofectin only one had fibres positive for dystrophin when examined 14 days later. Six pups were injected directly with full-length gene construct and when biopsies were taken 10 days later two of the animals had strongly stained peripheries to a small number of fibres.

L22 ANSWER 17 OF 50 MEDLINE on STN DUPLICATE 10

97159158. PubMed ID: 9006499. A new immunocompetent murine model for oral cancer. O'Malley B W Jr; Cope K A; Johnson C S; Schwartz M R. (Department of Otolaryngology-Head and Neck Surgery, Johns Hopkins University, Baltimore, Md, USA.) Archives of otolaryngology--head & neck surgery, (1997 Jan) 123 (1) 20-4. Journal code: 8603209. ISSN: 0886-4470. Pub. country: United States. Language: English.

AB OBJECTIVE: To develop and characterize a new immunocompetent murine model that attempts to parallel the clinical and biological nature of head and neck cancer. DESIGN: The growth rate and histologic characteristics of the SCC VII/SF cell line were initially determined in tissue culture experiments. Animal experiments were subsequently performed on C3H/HeJ mice. Using **direct injection**, 5 x 10(5) SCC VII/SF cells were delivered to the floor of the mouth of each animal. Animals were killed after 1, 2, and 3 weeks, and tumor growth, invasion, and regional and distant metastases were evaluated. RESULTS: Squamous cell carcinomas that could be palpated and measured externally were identified in the floor of the mouth of C3H/HeJ mice after 5 to 7 days. Local invasion into the mylohyoid musculature and mandible was present. Cervical **lymph node** and pulmonary metastases were identified between 2 and 3 weeks. CONCLUSIONS: This study introduces a new oral cancer animal model that shows initial locoregional tumor invasion, direct extension into the neck, early cervical metastases, and pulmonary metastases. These clinical and histopathologic attributes

reflect the biological behavior and tumor progression seen in human oral cancer and therefore provide a model for clinically applicable research for primary and metastatic head and neck cancer.

L22 ANSWER 18 OF 50 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

95288854 EMBASE Document No.: 1995288854. Locoregional immunotherapy - Topics at the 13th and 14th meeting of the Japanese Research Society for Surgical Cancer Immunology. Amano S.; Kurosu Y.; Shibata M.. First Department of Surgery, Nihon University School of Medicine, 30-1 Oyaguchi-Kamimachi,Itabashi-ku, Tokyo 173, Japan. Biotherapy 9/7 (845-851) 1995. ISSN: 0914-2223. CODEN: BITPE. Pub. Country: Japan. Language: Japanese. Summary Language: English; Japanese.

AB Seventy papers concerning locoregional immunotherapy were presented at the 1992.apprx.1993 meetings. The subjects were head and neck cancer, breast cancer, lung cancer, gastric cancer, liver cancer, colon cancer, metastatic cancer, peritonitis carcinomatosa and experimental animal tumors. The methods of administration of BRMs were **direct injection** into the tumor or the regional **lymph nodes**, or infusion into the hepatic artery or portal vein. Various BRMs were used (OK-432, PSK lentinan, IL-2, TNF, IFN-γ, and mono-clonal antibody, such as missile therapy). New and hopeful challenges have been launched to overcome cancer growth, using the new techniques developed in the field of molecular biology, for example.

L22 ANSWER 19 OF 50 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

95182130 EMBASE Document No.: 1995182130. Induction of cellular, but not humoral, tolerance to ovalbumin by **direct injection** into digestive tract segments or mesenteric **lymph nodes** in mice. Louis E.J.; Lamproye A.M.; Franchimont D.; Van Kemseke C.; Schaaf N.; Mahleu P.; Belaiche J.. Department of Gastroenterology, CHU of Liege, Domaine Universitaire du Sart Tilman,4000 Liege, Belgium. Regional Immunology 6/4 (251-256) 1994.
ISSN: 0896-0623. CODEN: REGIE3. Pub. Country: United States. Language: English. Summary Language: English.

AB The mechanism of systemic tolerance induction after feeding a protein antigen is poorly understood. In particular, the functions of different segments of the digestive tract, the mucosa, and the mesenteric **lymph nodes** are poorly understood. Moreover, recent studies have shown phenotypical and functional differences between mucosal lymphocytes of the small bowel and the colon. We investigated the effect of preimmunization with ovalbumin, given orally or administered directly into different digestive tract segments or into the mesenteric **lymph nodes**, on the subsequent systemic immune response to this antigen. As with oral preimmunization, we found that these routes of preimmunization induced cellular systemic tolerance, but unlike oral preimmunization they did not induce humoral systemic tolerance. These results confirm induction of humoral and cellular tolerance after feeding a protein antigen; they also confirm that cellular and humoral tolerance may be dissociated under some circumstances. They further show that cellular systemic tolerance may be induced at different levels of the digestive tract, and that several steps may be involved in its induction by feeding a protein antigen. On the other hand, humoral systemic tolerance seems to be more specific for oral preimmunization, suggesting a role for intraluminal degradation or possibly for a particular timing of presentation of the antigen in this phenomenon. Finally, we failed to show a difference between the small bowel and the colon regarding the effect of local preimmunization with ovalbumin on the subsequent systemic immune response to this antigen, despite the functional and phenotypical differences recently described.

L22 ANSWER 20 OF 50 MEDLINE on STN DUPLICATE 11

94107863. PubMed ID: 8280708. A genetic approach to idiotypic vaccination. Hawkins R E; Winter G; Hamblin T J; Stevenson F K; Russell S J. (MRC

Laboratory of Molecular Biology and Centre for Protein Engineering, Cambridge, United Kingdom.) Journal of immunotherapy : official journal of the Society for Biological Therapy, (1993 Nov) 14 (4) 273-8. Journal code: 9102704. ISSN: 1053-8550. Pub. country: United States. Language: English.

AB Treatment of cancer with vaccines is an attractive prospect, but few tumours express suitable target antigens. With B-cell lymphomas, the idiotypic immunoglobulin (Ig) of the malignant B-cell should provide a suitable target but this requires a vaccine to be created for each patient. We propose a strategy for making such vaccines: first to clone the V genes of the idiotypic Ig, and second to inject the patient with the cloned DNA (genetic immunisation) in order to elicit an immune response against the encoded Ig. We have previously shown that the V genes of the idiotypic Ig can be identified from human **lymph node** biopsies by polymerase chain reaction amplification, cloning, and sequencing. In this report, we show that anti-idiotypic antibodies can be elicited by **direct injection** of an expression vector that encodes the V genes of murine antibodies (the V genes of B1.8, a murine hybridoma or of BCL1, a murine lymphoma line). This finding suggests a simple approach to the preparation of idiotypic vaccines for patients with B-cell lymphoma, which also circumvents the need for adjuvants.

L22 ANSWER 21 OF 50 CAPLUS COPYRIGHT 2004 ACS on STN

1993:465 Document No. 118:465 Study on immune response of lymphocytes in the regional **lymph nodes** of gastric cancer by **direct injection** of active charcoal-adsorbed β (1→3) glucan. Shibata, Kazunari; Suzuki, Kazunobu; Tsurui, Shigeru; Tanifuji, Kiminori (Dep. Surg., Tokyo Med. Coll., Tokyo, Japan). Tokyo Ika Daigaku Zasshi, 50(3), 443-53 (Japanese) 1992. CODEN: TIDZAH. ISSN: 0040-8905.

AB Via an endoscope, active charcoal-adsorbed lentinan, lentinan, and active charcoal were locally applied to foci in 65 patients with curatively resectable gastric cancer before surgery, in an attempt to improve antitumoral activity of lymphocytes on the regional **lymph nodes** and to prevent malignant disease course progression. The resulting immune response was then evaluated by determining the functions of **lymph nodes** by measuring the ratio of the composition of various T cell subgroups, IL-2 production, LAK cell activity, and NK cell activity. Lentinan reinforced with adsorptive active charcoal particles had superior high lymph specificity and exerted a slow-release effect by accumulating in the regional **lymph nodes** via the lymph flow. In addition, this type of lentinan proved more effective than locally or systemically applied lentinan for increasing the immunol. competence of group I **lymph nodes** and raising lymphocyte antitumoral activity. Thus, supplementing lentinan with adsorptive active charcoal particles and locally applying it may be effective for preventing tumor metastasis.

L22 ANSWER 22 OF 50 MEDLINE on STN

93143457. PubMed ID: 1843434. [Anatomy and topography of external iliac **lymph nodes** in adults]. Anatomiia i topografiia naruzhnykh podvzdoshnykh limfaticheskikh uzlov u vzroslogo cheloveka. Shvetsov E V. Arkhiv anatomii, gistologii i embriologii, (1991 Jul-Aug) 100 (7-8) 50-7. Journal code: 0370603. ISSN: 0004-1947. Pub. country: RUSSIA: Russian Federation. Language: Russian.

AB The investigation of the external iliac **lymph nodes** has been performed in 152 preparations of corpses of mature persons of both sex, who died from causes not connected with any disease of the lymphatic system, lower extremities and pelvic organs. The external iliac **lymph nodes** and their afferent and efferent lymphatic vessels have been revealed by means of interstitial injection of the lower extremities and pelvic organs, as well as by means of **direct injection** of Gerota mass into the lymphatic vessels. Form, amount, dimensions and topography of common iliac **lymph**

nodes have been studied. Lymphatic vessels, running from certain parts and organs of the body to various subgroups of the external iliac **lymph nodes** have been described, as well as efferent lymph vessels of these nodes. The external iliac **lymph nodes** are constant formations; the largest of them--**lymph nodes** of the lacuna--are nodes of the I step for the lower extremity lymph vessels. In 54% of cases in persons of both sex positive (right-sided) asymmetry has been revealed. Total amount of the iliac **lymph nodes** prevails in men, while their size is greater in women. The size of these nodes in persons of both sex is greater to the left than to the right. There are connections (in 3% of cases) between the external iliac **lymph nodes** and aortal and lumbar nodes of the opposite side.

L22 ANSWER 23 OF 50 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
1993:339492 Document No.: PREV199396036492. Anatomy and topography of external iliac lymph **nodes** in adults. Shvetsov, E. V.. Div. Anat. Human, I.M. Sechenov Mosc. Med. Acad., Moscow, Russia. Arkhiv Anatomii Gistologii i Embriologii, (1991) Vol. 100, No. 6-8, pp. 50-57. CODEN: AAGEAA. ISSN: 0004-1947. Language: Russian.

AB The investigation of the external iliac **lymph nodes** has been performed in 152 preparations of corpses of mature persons of both sex, who died from causes not connected with any disease of the lymphatic system, lower extremities and pelvic organs. The external iliac **lymph nodes** and their afferent and efferent lymphatic vessels have been revealed by means of interstitial injection of the lower extremities and pelvic organs, as well as by means of **direct injection** of Gerota mass into the lymphatic vessels. Form, amount, dimensions and topography of common iliac **lymph nodes** have been studied. Lymphatic vessels, running from certain parts and organs of the body to various subgroups of the external iliac **lymph nodes** have been described, as well as efferent lymph vessels of these nodes. The external iliac **lymph nodes** are constant formations; the largest of them - **lymph nodes** of the lacuna - are nodes of the I step for the lower extremity lymph vessels. In 54% of cases in persons of both sex positive (right-sided) asymmetry has been revealed. Total amount of the iliac **lymph nodes** prevails in men, while their size is greater in women. The size of these nodes in persons of both sex is greater to the left than to the right. There are connections (in 3% of cases) between the external iliac **lymph nodes** and aortal and lumbar nodes of the opposite side.

L22 ANSWER 24 OF 50 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 12
1989:430235 Document No.: PREV198988088493; BA88:88493. IMMUNOSUPPRESSIVE EFFECT OF A SMALL DOSE OF CYCLOSPORINE DIRECTLY INJECTED INTO THE THORACIC DUCT COMBINED WITH SPLENECTOMY ON SURVIVAL OF RAT KIDNEY ALLOGRAFT. NAKAJI K [Reprint author]. SECOND DEP SURG, KYOTO PREFECTURAL UNIV MED. Journal of Kyoto Prefectural University of Medicine, (1989) Vol. 98, No. 7, pp. 745-754.
CODEN: KFIZAO. ISSN: 0023-6012. Language: JAPANESE.

AB Immunosuppressive effect of CsA directly injected into the thoracic duct, which had been ligated 3 days before, with or without splenectomy was examined in rat renal allograft model. Single injection of a small dose of CsA (4 mg/kg) into thoracic duct prolonged graft survival to 14.8 ± 4.6 days (n = 8) significantly, as compared with control group (9.3 ± 1.4 days, n = 9). Furthermore, combined treatment of **direct injection** of CsA into the thoracic duct and splenectomy yielded significantly longer graft survival to 22.9 ± 7.7 days (n = 7), as compared with CsA injection group (14.8 ± 4.6 days, p< 0.025) or splenectomy group (13.5 ± 4.1 days, <0.025). It is likely that this long graft survival was achieved due to suppression of activity of effector lymphocytes derived from the lymphnodes which kept in contact with selectively localized highly concentrated CsA in the thoracic duct,

and due to inhibition of cytotoxic antibody production by concomitant splenectomy. These results suggest that **direct injection** of CsA into the thoracic duct has a beneficial effect allowing a reduction in therapeutic CsA dosage and its side effects.

L22 ANSWER 25 OF 50 MEDLINE on STN DUPLICATE 13
89117359. PubMed ID: 3219074. [Individual and sexual characteristics of the common iliac **lymph nodes** in elderly persons]. Individual'nye i polovye osobennosti obshchikh podvzdoshnykh limfaticheskikh uzlov u liudei pozhologo vozratsa. Shvetsov E V. Arkhiv anatomii, gistologii i embriologii, (1988 Sep) 95 (9) 53-8. Journal code: 0370603. ISSN: 0004-1947. Pub. country: USSR. Language: Russian.

AB The common iliac **lymph nodes** (CILN) have been investigated on 24 preparations from corpses of elderly persons (5 male and 7 female corpses), died from the causes not connected with the lymphatic system diseases, lower extremities and pelvic organs. The CILN with their afferent and deferent lymphatic vessels are revealed by means of interstitial injection into the lower extremities and pelvic organs, as well as by means of **direct injection** into lymphatic vessels. The form, amount, size and topography of CILN are studied. Lymphatic vessels, running from certain parts of the body and organs to various subgroups of CILN are described, as well as lymphatic vessels, connecting the nodes both within each subgroup and between the subgroups. There is a tendency in prevalence of amount and size of the lateral subgroup of the **lymph nodes** over the nodes of other subgroups of CILN; tendency in prevalence of amount of the **lymph nodes** in men, and their size--in women; prevalence of amount of right CILN and their size in the left--in persons of both sex; in 70% of the cases the amount of afferent lymphatic vessels to CILN prevails over that of the deferent **lymph nodes.**

L22 ANSWER 26 OF 50 MEDLINE on STN DUPLICATE 14
88113762. PubMed ID: 3428927. Distribution of lung-associated lymphocytes from the caudal mediastinal **lymph node**: effect of antigen. Joel D D; Chanana A D. (Medical Department, Brookhaven National Laboratory, Upton, NY 11973.) Immunology, (1987 Dec) 62 (4) 641-6. Journal code: 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Lymphocytes from the efferent lymph of the caudal mediastinal **lymph node** (CMLN) were labelled in vitro with 125I-iododeoxyuridine [125I]UdR and Na2(51)CrO4. The labelled cells were re-infused i.v. and their distribution in organs/tissues was determined 20-24 hr later. As indicated by tissue 125I-activity, pulmonary lymphoblasts had a marked tendency to relocate in the lung, regional pulmonary **lymph nodes** and spleen. Localization of efferent CMLN lymphoblasts was greater in antigenically stimulated segments compared to unstimulated segments of the lung. Dual antigen experiments indicated that the increased localization was not specific for the antigen which stimulated production of lymphoblasts used for in vitro labelling and reinfusion. Intranodal labelling of blasts by the **direct** injection of [125I]UdR supported the results obtained from in vitro labelling. In these studies, comparisons were made with the localization of lymphocytes obtained from thoracic duct lymph.

L22 ANSWER 27 OF 50 MEDLINE on STN DUPLICATE 15
88048928. PubMed ID: 3675209. [Anatomy and topography of the common iliac **lymph** nodes in human beings in the 1st period of maturity]. Anatomiia i topografiia obshchikh podvzdoshnykh limfaticheskikh uzlov u liudei pervogo perioda zrelogo vozrasta. Shvetsov E V. Arkhiv anatomii, gistologii i embriologii, (1987 Jul) 93 (7) 33-7. Journal code: 0370603. ISSN: 0004-1947. Pub. country: USSR. Language: Russian.

AB The investigation of common iliac **lymph nodes** has been performed in 20 corpses of the first mature age of both sex (5 male and 5 female corpses) of persons died from causes not connected with the

lymphatic system diseases, the lower extremities and the pelvic organs. The common iliac **lymph nodes** with their afferent and efferent lymphatic vessels are revealed by means of interstitial injection into the lower extremities and the pelvic organs and with **direct injection** into the lymphatic vessels. The form, amount, size and topography of the common iliac lymphatic vessels have been studied. The lymphatic vessels, that go from certain body parts and organs to various subgroups of the common iliac **lymph nodes**, as well as the lymphatic vessels that connect the nodes both within the subgroup and also between the subgroups. The amount and size of the lymphatic nodes of the lateral subgroup predominate over the nodes of other subgroups of the common iliac **lymph nodes**; the amount of the common iliac **lymph nodes** predominates in men, and their size--in women. Amount of these nodes in the right and their size in the left predominate in both sex. Among the common iliac **lymph nodes** there are no teniform nodes, and efferent lymphatic vessels of the lateral and medial subgroup of the common iliac **lymph nodes** in 15% of cases run towards the lumbar nodes in the opposite side.

L22 ANSWER 28 OF 50 MEDLINE on STN DUPLICATE 16
86272442. PubMed ID: 3731379. The role of the Peyer's patch in carcinogenesis. I. The adsorption from the gut and retention of 3-methylcholanthrene by Peyer's patches. Bost K L; Cuchens M A. Carcinogenesis, (1986 Aug) 7 (8) 1251-6. Journal code: 8008055. ISSN: 0143-3334. Pub. country: United States. Language: English.

AB Radiotracer methods were used to determine the distribution of 3-methylcholanthrene (3-MC) within the lymphoid organs of rats following i.g. intubation, i.l. injection into the small intestine, i.v. injection or **direct injection** of the Peyer's patches with 3-[6-14C]methylcholanthrene (14C-MC). The data indicate that the gut-associated Peyer's patches and mesenteric **lymph nodes** were exposed to higher amounts of orally administered 14C-MC than any of the other lymphoid organs. Whereas the Peyer's patches exhibited the highest sp. act. for longer periods of time when low amounts of 14C-MC were administered, the sp. act. of the mesenteric **lymph node** was greater when rats were intubated with higher amounts of 14C-MC. Furthermore, the Peyer's patches were exposed to higher amounts of possible metabolites of 14C-MC. Injection of 14C-MC into the small intestinal lumen resulted in increased ratios of the Peyer's patch sp. act. to mesenteric **lymph node** sp. act., indicating that by-passing the stomach altered the distribution patterns. Data from rats injected i.v. with 14C-MC demonstrated that mesenteric **lymph nodes** but not Peyer's patches adsorbed and retained 14C-MC from the blood and indicated that the 14C-MC associated with Peyer's patches of i.g. intubated rats was adsorbed from the gut rather than from the blood. Results obtained from rats which were exposed to 3-MC by directly injecting Peyer's patches with 14C-MC also indicated that the Peyer's patches were able to retain 3-MC once localized within this lymphoid organ, to metabolize the 3-MC and to possibly excrete the polycyclic aromatic hydrocarbon into the small intestine. Collectively the data indicate that Peyer's patches have an important role in the adsorption from the gut and subsequent retention of 3-MC and hence may be a likely target organ for lymphoid carcinogenesis following oral exposure to carcinogenic polycyclic aromatic hydrocarbons.

L22 ANSWER 29 OF 50 MEDLINE on STN DUPLICATE 17
86105673. PubMed ID: 3943008. Salvage of stage IV intraoral squamous cell carcinomas with preoperative 5-fluorouracil. Ryan R F; Krementz E T; Truesdale G L. Cancer, (1986 Feb 15) 57 (4) 699-705. Journal code: 0374236. ISSN: 0008-543X. Pub. country: United States. Language: English.

AB A regimen for improving the salvage rate for Stage IV squamous cell carcinoma of the tongue, alveolar ridge and floor of mouth is presented. This method utilizes pre-operative sensitization of the tumor and regional **lymph nodes** by the topical application of 5-fluorouracil

(5-FU) in the form of Efudex (Roche). The drug must be used topically at the tumor skin or tumor-mucous membrane interface to utilize the sensitizing properties of skin or mucous membrane. Further response is obtained by **direct injections** of 5-FU into the tumor. Later intravenous (IV) drip of 5-FU can be used particularly at the time of surgical resection. During the period of preparation until sensitized to 5-FU, patients must be restored to positive nitrogen balance and concurrent infections are controlled. Because of the importance of nutrition in restoring immunity, a feeding gastrostomy for these patients is recommended. The definitive surgery must include all bone that is involved, as 5-FU alone will not sterilize the bone. Of 15 patients who underwent the regimen outlined in this study, 12 of the patients with Stage IV intra-oral squamous cell carcinoma have had their primary tumor controlled for 17 months to 5 years at the time of this report.

L22 ANSWER 30 OF 50 MEDLINE on STN
87093952. PubMed ID: 3797998. Corrosion cast technique applied in lymphatic pathways. Castenholz A. Scanning electron microscopy, (1986) (Pt 2) 599-605. Journal code: 0371617. ISSN: 0586-5581. Pub. country: United States. Language: English.
AB The paper deals with methods and results of the microcorrosion cast technique in lymph angiology. For the representation of the special organization of the lymph vascular system including the initial vascular structures, intranodal pathways, bigger collectors, and lymph trunks, the application of various injection techniques is necessary. The interstitial injection of Mercox proves to be suitable to show the initial lymphatics and prelymphatic spaces. Similarly, the intranodal injection makes visible the system of the lymph sinuses and the spaces of the reticular tissue in this organ. Casts of bigger collecting vessels, lymph trunks, and thoracic duct can be obtained by **direct injection** of the resin into the vascular lumen. Thus, these techniques enable to make visible the structural details of the cast preparations of all parts of the lymphatic system.

L22 ANSWER 31 OF 50 MEDLINE on STN
84178034. PubMed ID: 6712496. [Anatomy and topography of the lymphatic vessels and regional **lymph nodes** of the rectum in newborn infants and children to 3 years of age]. Anatomiia i topografiia limfaticheskikh sosudov i regionarnykh limfaticheskikh uzlov priamoi kishki u novorozhdennykh i detei do 3 let zhizni. Abdykerimov S A. Arkhiv anatomii, gistologii i embriologii, (1984 Feb) 86 (2) 65-9. Journal code: 0370603. ISSN: 0004-1947. Pub. country: USSR. Language: Russian.
AB In 30 corpses of newborns and children up to 3 years of age, by means of the intratissue and **direct injection** of the modified Gerota's mass, certain increase in number and size of the superficial inguinal lymph vessels belonging to the superior-medial group, as well as the pararectal and superior rectal **lymph nodes** has been noted. The diameter of both afferent and efferent lymphatic vessels in the nodes mentioned in children of 1-3 years of age is greater than in the newborns. The number of the afferent vessels running towards these nodes in most cases, regardless the age, prevail over the efferent ones, and the diameter of the latter is greater than in the afferent vessels. The pararectal **lymph nodes** in 80% of cases are the nodes of the first step for the lymph flowing from the rectum, in 15% - the nodes of the first and second steps, simultaneously, and in 5% - of the third and fourth steps. The superior pararectal **lymph nodes** in 80% of cases are the nodes of the third and fourth steps, and in 20% of cases - those of the first and second steps for the lymph flowing from the rectum.

L22 ANSWER 32 OF 50 CAPLUS COPYRIGHT 2004 ACS on STN
1984:79567 Document No. 100:79567 Experimental study of local chemotherapy with topical injection of adriamycin. Muto, Fumitaka (1st Dep. Surg., Kyoto Prefect. Univ. Med., Kyoto, Japan). Kyoto-furitsu Ika Daigaku Zasshi, 92(12), 2027-36 (Japanese) 1983. CODEN: KFIZAO. ISSN: 0023-6012.

AB Local application of adriamycin [23214-92-8] is more efficient than i.v. injection in controlling **lymph node** metastasis and minimizing toxic side effects. This was demonstrated by injecting the drug into rat gastric mucosa and showing a high concentration of the drug in the stomach for a prolonged period with little toxic effect on the stomach. The concentration of adriamycin in the liver was considerably less than that observed after i.v. injection. In rats bearing AH-130 tumor in the foot pad, **direct injection** of adriamycin into the tumor increased the survival rate and had a greater efficacy than did the i.v. injection.

L22 ANSWER 33 OF 50 MEDLINE on STN DUPLICATE 18
83121323. PubMed ID: 6218666. T cell help in cytotoxic T lymphocyte response. Role of the I region in helper cell induction. Livnat S; Corley R B. Transplantation, (1983 Jan) 35 (1) 78-83. Journal code: 0132144. ISSN: 0041-1337. Pub. country: United States. Language: English.
AB We have studied the in vivo induction of T helper (TH) cells that participate in the generation of cytotoxic T (TC) lymphocytes. Helper activity was measured by the ability of the cells to help resting thymic TC cell precursors develop into effector TC cells in vitro. **Direct injection** of allogeneic spleen cells into the footpads of mice led to the generation of alloantigen-specific helper cells in the draining popliteal **lymph nodes** within 4 to 6 days. Helper activity was mediated by nylon-wool-nonadherent Lyt-1+ T lymphocytes; some activity was associated with Lyt-1,2+ cells. The genetic requirements for both the induction and restimulation of C3H anti-H-2d TH cells were investigated using cells from H-2k/H-2d recombinant mice as in vivo immunogens and in vitro stimulators. Evidence is presented that shows in a direct assay that TH cells themselves are specific for I region-coded determinants. Thus, disparity at the left side of the H-2 complex (K to I-E) but not at H-2K alone was necessary and sufficient to induce and reactivate TH cells. Proliferation in mixed lymphocyte culture was measured in combinations in which TH cells were not detectable, supporting the idea that proliferation cannot be strictly considered a measurement of helper cells.

L22 ANSWER 34 OF 50 MEDLINE on STN DUPLICATE 19
82283346. PubMed ID: 7115115. [Anatomy and topography of human bronchopulmonary **lymph nodes**]. Anatomiia i topografiia bronkholegochnykh limfaticheskikh uzlov u cheloveka. Aubakirov A B. Arkhiv anatomii, gistologii i embriologii, (1982 Jun) 82 (6) 84-7. Journal code: 0370603. ISSN: 0004-1947. Pub. country: USSR. Language: Russian.
AB In 48 corpses of persons at the age 17-76 years (28 men and 20 women) anatomy and topography of the bronchopulmonary **lymph nodes** have been described. The nodes studies have been revealed by means of interstitial and **direct injection** of Gerota mass into the pulmonary tissues and lymphatic vessels with a subsequent macro- and micropreparation of the **lymph nodes** beside the bronchopulmonary **lymph node** subgroups described previously (posterior, inferior, anterior, superior), left and right interlobular bronchopulmonary **lymph nodes** have been revealed situating in the angles where the lobular bronchi branch off the left and right main bronchi, as well as on surfaces of the lobular bronchi turned towards the interlobular fissures. The left interlobular and upper bronchopulmonary **lymph nodes** are the most frequent occurrence. The left and right superior bronchopulmonary **lymph nodes** occur in a greater number than **lymph nodes** in other subgroups. The size of the bronchopulmonary **lymph nodes** varies within a wide range. The form of the nodes depends on the place of their localization.

L22 ANSWER 35 OF 50 MEDLINE on STN DUPLICATE 20
83021796. PubMed ID: 7125916. [Variants in the number and size and the topography of the lumbar **lymph nodes** in the regional

of the liver in the human adult]. Varianty kolichestva, razmerov i topografiia regionarnykh dlia pecheni poiasnichnykh limfaticheskikh uzlov u vzroslogo cheloveka. Usovich A K; Borziak E I. Arkhiv anatomii, gistologii i embriologii, (1982 Jul) 83 (7) 29-33. Journal code: 0370603. ISSN: 0004-1947. Pub. country: USSR. Language: Russian.

AB By means of interstitial and **direct injections** of the lymphatic bed of the liver and gall bladder, their regional **lymph nodes** from the lumbar group have been studied in 63 corpses of mature persons of both sex. The hepatic lymph vessels flow into the lumbar **lymph nodes** in 73% of cases. Only the postaortal nodes (situating behind the abdominal part of the aorta) do not take the hepatic **lymph nodes.** The number of the hepatic regional lumbar **lymph nodes** varies from 1 to 6, and their size is within the limits 2X2--30X10 mm. In 13% of cases intermediate lumbar **lymph nodes** have been revealed (6X4 mm in size), they are situated along the pathway of the visceral surface of the lymph vessels (of the right hepatic lobe) running towards large intermediate lumbar **lymph nodes.**

L22 ANSWER 26 OF 50 MEDLINE on STN DUPLICATE 21

82051808. PubMed ID: 6795108. In vivo labelling of the spleen and mesenteric **lymph** nodes with fluorescein isothiocyanate for lymphocyte migration studies. Pabst R; Binns R M. Immunology, (1981 Oct) 44 (2) 321-9. Journal code: 0374672. ISSN: 0019-2805. Pub. country: ENGLAND, United Kingdom. Language: English.

AB Lymphocytes in normal young pigs were labelled in vivo with fluorescein isothiocyanate in the spleen using an extracorporeal perfusion system and in mesenteric **lymph nodes** by **direct injection** into the nodes. Labelled lymphocytes leave the spleen at a high rate via the splenic vein and migrate to different lymphoid organs. Emigrants from mesenteric **lymph nodes** left the nodes more slowly and revealed a different homing pattern. Evidence is presented that a considerable number of lymphocytes from the parenchyma leave the nodes via the vein and not by the classical route of recirculating lymphocytes via the efferent lymphatics. Fluorescein labelling of lymphocytes in their normal micro-environment is a suitable method for lymphocyte migration studies.

L22 ANSWER 27 OF 50 MEDLINE on STN DUPLICATE 22

81020592. PubMed ID: 7416982. [Anatomy and topography of adult human mesenteric **lymph nodes**]. Anatomiia i topografiia bryzhzhevykh limfaticheskikh uzlov vzroslogo cheloveka. Sapin M R; Borziak E I; Makhmudov Z A. Arkhiv anatomii, gistologii i embriologii, (1980 Jun) 78 (4) 60-4. Journal code: 0370603. ISSN: 0004-1947. Pub. country: USSR. Language: Russian.

AB Topography, number and age changes of the mesenteric **lymph nodes** of the small intestine have been studied in 40 corpses of both sexes of the age of 21-90 years. The mesenteric **lymph nodes**, their afferent and deferent vessels have been revealed by the method of intersticial injection of coloured masses into the small intestinal wall, as well as by a **direct injection** of the **lymph nodes** studied in the mesentery. Variability in the total number of the mesenteric **lymph nodes** has been demonstrated; topographic borders of separate groups of the mesenteric **lymph nodes** have been stated; topography of the **lymph nodes** as regards the mesenteric blood vessels has been described. Quantitative changes (total and group) in the mesenteric **lymph nodes** with age in grown-up persons have been demonstrated.

L22 ANSWER 28 OF 50 MEDLINE on STN DUPLICATE 23

79165172. PubMed ID: 435101. [Anatomical variants of the lymphatic vessels connecting the inguinal **lymph nodes**]. Varianty anatomicheskikh limfaticheskikh sosudov, soediniaiushchikh pakhovye limfaticheskie uzly. Shvetsov E V; Sapin M R. Arkhiv anatomii, gistologii

i embriologii, (1979 Mar) 76 (3) 51-7. Journal code: 0370603. ISSN: 0004-1[illegible]. Pub. country: USSR. Language: Russian.
AB The stu[illegible] of anatomical variants of lymphatic vessels connecting inguinal **lymph n**[illegible]s was carried out on 56 corpses of adult persons [illegible]f both sex whose deaths were not connected with lesions in the lymphatic system of the pelvis and lower extremities. The inguinal **lymph no**[illegible]es and their afferent and efferent lymphatic vessels [illegible]ere detected by the method of intradermal injection and by the method o[illegible] **direct injection** into the lymphatic vessels. It was [illegible]tated that groups of the inguinal **lymph nodes**, as well [illegible]s the nodes in every group determined, can serve as nodes of differe[illegible] stages for afferent lymphatic vessels running from different parts o[illegible] the body and organs.

L22 ANSWER [illegible] OF 50 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
78302393 EMBASE Document No.: 1978302393. Visualization of paravesical lymphati[illegible]s by **direct injection** of contrast medium. Fiorelli[illegible] C.; Lunghi F.; Nicita G.; et al.. Dept. Urol., Univ. Florence, Italy. U[illegible]ology 11/2 (200-202) 1978. CODEN: U[illegible]GYAZ. Pub. Country: United States. Language: English.
AB Several [illegible]ontrast media were injected endoscopically into the bladder of 10 patients. Satisfactory visualization of the paravesical lymphatics occurred in some cases. This was due to the physical properties of iodine compound[illegible] and their degree of lymphatic absorption.

L22 ANSWER [illegible] OF 50 MEDLINE on STN DUPLICATE 24
77097326. [illegible]ubMed ID: 189098. Testicular lymphography: clinical study. Gandhi M[illegible]G. Journal of urology, (1977 Feb) 117 (2) 174. Journal code: 0376374. [illegible]SSN: 0022-5347. Pub. country: United States. Language: English.
AB **Direct** [illegible]**ction** of lipiodol into the parenchyma of the hum[illegible] testis to study retroperitoneal lymphatics and **lymph nodes** i[illegible] a potentially dangerous investigation. The information obtaine[illegible] with this study is incomplete and far inferior when compared to result[illegible] obtained with standard procedures, such as pedal lymphography or cannula[illegible]ion of testicular lymphatics.

L22 ANSWER [illegible] OF 50 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
78048302 EMBASE Document No.: 1978048302. Testicular lymphography: clinical study. G[illegible]ta Gandhi M.. Governm. Gen. Hosp., Gulbarga, India. Journal of Urology [illegible]17/2 (174) 1977. CODEN: [illegible]URAA. Language: English.
AB **Direct** [illegible]**ction** of lipiodol into the parenchyma of the hu[illegible] testis to study retroperitoneal lymphatics and **lymph nodes** [illegible] a potentially dangerous investigation. The information obtain[illegible] with this study is incomplete and far inferior when compared to result[illegible] obtained with standard procedures, such as pedal lymphography or cannula[illegible]ion of testicular lymphatics.

L22 ANSWER [illegible] OF 50 MEDLINE on STN DUPLICATE 25
76135160. [illegible]ubMed ID: 1252142. [Age and variability in the inguinal **lymph** n[illegible]s of adult humans]. Vozrastnaia izmenc[illegible]ost' pakhovykh limafaticheskikh uzlov u vzroslogo cheloveka. Shvets[illegible]E V. Arkhiv anatomii, gistologii i embriologii, (1976 Jan) 70 (1) 73-7. [illegible]urnal code: 0370603. ISSN: 0004-1947. Pub. country: USSR. Langu[illegible]: Russian.
AB Lymph[illegible] nodes on the anterior surface of the femur, in the region of the femor[illegible] triangle were studied in 56 corpses of humans of either sex from 31 to [illegible] years of age, dead of accidental causes or of diseases not related [illegible] lymphatic nodes. The investigation was carried on by the method o[illegible] interstitial and **direct injection** of the Gerota's [illegible]ss to some regions of foot skin, external genitalia and the skin of [illegible] anterior wall of the abdomen. It has been established that the si[illegible] of inguinal lymphatic nodes (both superficial and profound) in

humans of either sex, are in direct dependence on the age of the person. The amount of inguinal lymphatic nodes in young people prevails over that in old people. The external diameter of the afferent and efferent vessels in elderly humans is greater than in young ones. The amount of afferent lymphatic vessels to inguinal lymphatic nodes in most cases prevails over the amount of efferent ones, independent of age and sex. The external diameter of the former is greater than that of the latter.

L22 ANSWER 43 OF 50 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

74210138 EMBASE Document No.: 1974210138. [**Lymph nodes** and lymphatics of the pelvis and the pelvic limb of the goat]. DIE LYMPHKNOTEN UND LYMPHGEFASSE DES BECKENS UND DER BECKENGLIEDMASSE DER ZIEGE. Nickel R.; Schummer A.; Seiferle E.; Wilkens H.; Frewein J.. Inst. Makrosk. Anat. Tiere, Univ. Munchen, Germany. BERL.MUNCH.TIERARZTL.WSCHR. 87/6 (101-105) 1974. CODEN: BMTAM. Language: German.

AB The **lymph nodes** of the pelvis and the pelvic limb were examined in 46 goats of different breeds and different ages. Many of the afferent lymphatics were visualized by injection of a mixture of Indian ink and water or Indian ink and serum into the subcutis, into fascias, tendons, tendon sheaths, joint capsules and ligaments. The efferent lymphatics were filled by **direct injection** into the **lymph nodes**. The following **lymph nodes** are always present: Ln. popliteus, Ln. ischiadicus, Ln. inguinalis superficialis, Ln. subiliacus, Lnn. iliaci mediales, and Ln. sacralis. Not always present are: Ln. tuberalis Ln. inguinalis profundus, and Ln. hypogastricus.

L22 ANSWER 44 OF 50 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

74124958 EMBASE Document No.: 1974124958. Direct and indirect plaque forming cells in extrapulmonary lymphoid tissue following local vs systemic injection of soluble antigen. Nash D.R.. East Texas Chest Hosp., Tyler, Tex. 701, United States. Cellular Immunology 9/2 (234-241) 1973. CODEN: CLIMB8. Language: English.

AB AKR strain mice were immunized with solubilized SRBC stroma either by **direct injection** into the lower respiratory tract or intravenously via the tail vein. The number of plaque forming cells (PFC) in the draining pulmonary **lymph node** (tracheobronchial node) and spleen were determined by direct (IgM) and indirect (IgG(1), IgG(2b), IgA) plaque assays. Intravenously administered antigen induced an initially strong IgM response in the spleen which was subsequently followed by antibody of the IgG(1), IgG(2b), and IgA classes of immunoglobulins. The tracheobronchial **lymph node** contained a minimal number of PFC representing all 4 types of immunoglobulins studied. Conversely, following a single local injection of antigen directly into the lower respiratory tract, the tracheobronchial node responded with relatively high concentrations of PFC of all classes. The response in the spleen, although higher than background, was barely detectable. The splenic response to locally administered antigen was, however, considerably augmented as a result of a second local injection given 5 days after the initial stimulation. Under these conditions, IgG(1), IgG(2b), and IgA were represented in both tissue sites by sharp increases in the number and a decrease in the time of appearance of their respective antibody forming cells. Comparable changes were not noted for the case of IgM. Serum hemagglutination titers following a single injection by either route did not vary significantly during the time course of the experiment (28 days). The sera from locally immunized mice were treated with the reducing agent dithiothreitol and hemagglutination titers before and after treatment, were compared. The major serum activity observed during the first 10 days following injection was affected by reduction and could therefore by assigned to high molecular weight antibody (19S, 13S). Subsequent titers (days 13-26) were less susceptible to DTT and are considered to represent low molecular weight immunoglobulins (7S).

L22 ANSWER 45 OF 50 CAPLUS COPYRIGHT 2004 ACS on STN
1969:489536 Document No. 71:89536 Two rapidly labeled RNA species in the polysomes of antibody-producing lymphoid tissue. Kuechler, Ernst; Rich, Alexander (Massachusetts Inst. of Technol., Cambridge, MA, USA). Proceedings of the National Academy of Sciences of the United States of America, 63(2), 520-7 (English) 1969. CODEN: PNASA6. ISSN: 0027-8424.

AB Popliteal **lymph nodes** of rabbits stimulated to produce antibodies were pulse labeled in vivo by **direct injection** of uridine-3H. RNA was then extracted from isolated polysomes and single ribosomes. Fractionation of this RNA by polyacrylamide-gel electrophoresis revealed the synthesis of 2 discrete peaks of labeled RNA migrating in the region between 18 S ribosomal and 4 S transfer RNA. These peaks were found in the RNA extracted from polysomes but were absent from single ribosomes. When the polysomes were disrupted by EDTA treatment the RNA species no longer appeared as rapidly sedimenting material. These 2 RNA's have mol. wts. near 2.2 + 105 and 3.7 + 105 daltons. The chemical and biol. properties of these species as well as the mol. wts. were consistent with those expected for monocistronic messenger RNA coding for the antibody L and H chains, resp.

L22 ANSWER 46 OF 50 CAPLUS COPYRIGHT 2004 ACS on STN
1968:450566 Document No. 69:50566 The production of high-titer antibody against free angiotensin II. Boyd, G. W.; Peart, W. S. (Med. Sch., St. Mary's Hosp., London, UK). Lancet, II(7560), 129-33 (English) 1968. CODEN: LANCAO. ISSN: 0140-6736.

AB A major difficulty in radioimmunoassay of small polypeptide hormones was the development of a suitable antibody. Most current techniques involve immunizing with peptide which has been chemical linked to a carrier protein. In the present study, specific antibodies to free angiotensin II were produced in high titer by immunization with angiotensin amide (hypertensin) which was adsorbed phys. onto microparticles of C. The **direct injection** of the immunizing mixture into **lymph nodes** and spleen probably was more effective in antibody production than i.m. or i.p. injection in rabbits. Regardless of the route of immunization, immune plasma or γ-globulin demonstrated a capacity to neutralize the biol. activity of angiotensin II extremely rapidly and effectively. The technique of adsorption of antigen on C may have great utility in the preparation of antibodies to other small peptides of biol. interest. Based on the antibody, a sensitive angiotensin immunoassay was developed. 27 references.

L22 ANSWER 47 OF 50 MEDLINE on STN
68353299 PubMed ID: 5664401. Evaluation of the **direct injection** of antigen into a peripheral **lymph node** for the production of humoral and cell-mediated immunity in the guinea-pig. Horne C H; White R G. Immunology, (1968 Jul) 15 (1) 65-74. Journal code: 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.

L22 ANSWER 48 OF 50 CAPLUS COPYRIGHT 2004 ACS on STN
1964:41316 Document No. 61:13803 Original Reference No. 61:2326g-h **Direct injection** of the thymus with antigenic substances. Sherman, Joseph D.; Adner, Marvin M.; Dameshek, William (Tufts Univ., Boston, MA). Proceedings of the Society for Experimental Biology and Medicine, 115(12), 866-70 (Unavailable) 1964. CODEN: PSEBAA. ISSN: 0037-9727.

AB **Direct injection** of the thymus gland of the adult hamster with a variety of substances (named), mostly of mammalian origin, produced changes in lymphoid tissues, bone marrow, and blood that suggested thymic stimulation. The changes produced include splenomegaly, increase of bone marrow lymphocytes, increase of γ-globulin, pos. Coombs' antiglobulin test, development of follicles within the thymus gland, plasma cell development within the thymus, spleen and **lymph nodes**, and anemia, possibly of the autoimmune type.

L22 ANSWER 49 OF 50 CAPLUS COPYRIGHT 2004 ACS on STN
1949:15666 Document No. 43:15666 Original Reference No. 43:3095b-e The development of tumors in various tissues in mice following direct application of a carcinogenic hydrocarbon. Rask-Nielsen, Ragna Acta Path. Microbiol. Scand., Suppl., 78, 1-144 (Unavailable) 1948.
AB **Direct injection** of a small amount of 9,10-dimethyl-1,2-benzanthracene into various organs of mice indicates that the thymus gland and lung are more susceptible than any of the other tissues which produce tumors spontaneously (subcutaneous tissue, skin, mammary tissue). **Direct injection** of large doses of this carcinogen into various organs induced tumors in thymus gland, lung, and also subcutaneous tissue but not in the other tissues capable of spontaneous tumor formation, or in those not capable of spontaneous tumor formation (**lymph nodes**, spleen, bone marrow, kidney and testis) with the exception of one testicular sarcoma. Nonlocal tumor formation was observed in thymus gland and lung, with leukemic infiltration only, in **lymph nodes** and spleen. Carcinogenic agents do not produce tumors in tissues incapable of the spontaneous generation of tumors.

L22 ANSWER 50 OF 50 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
1995:345903 Document No.: PREV199598360202. Induction of cellular, but not humoral, tolerance to ovalbumin by **direct injection** into digestive tract segments or mesenteric **lymph nodes** in mice. Louis, Edouard J. [Reprint author]; Lamproye, Annouk M.; Franchimont, Denis; Van Kemseke, Catherine; Schaaf, Nicole; Mahieu, Philippe; Pelaiche, Jacques. Dep. Gastroenterol. Immunol, CHU Liege, Domaine Univ. du Sart Tilman, 4000 Liege, Belgium. Regional Immunology, (1994 (95)) Vol. 6, No. 4, pp. 251-256. .
ISSN: 0896-0623. Language: English.
AB The mechanism of systemic tolerance induction after feeding a protein antigen is poorly understood. In particular, the functions of different segments of the digestive tract, the mucosa, and the mesenteric **lymph nodes** are poorly understood. Moreover, recent studies have shown phenotypical and functional differences between mucosal lymphocytes of the small bowel and the colon. We investigated the effect of preimmunization with ovalbumin, given orally or administered directly into different digestive tract segments or into the mesenteric **lymph nodes**, on the subsequent systemic immune response to this antigen. As with oral preimmunization, we found that these routes of preimmunization induced cellular systemic tolerance, but unlike oral preimmunization they did not induce humoral systemic tolerance. These results confirm induction of humoral and cellular tolerance after feeding a protein antigen; they also confirm that cellular and humoral tolerance may be dissociated under some circumstances. They further show that cellular systemic tolerance may be induced at different levels of the digestive tract, and that several steps may be involved in its induction by feeding a protein antigen. On the other hand, humoral systemic tolerance seems to be more specific for oral preimmunization, suggesting a role for intraluminal degradation or possibly for a particular timing of presentation of the antigen in this phenomenon. Finally, we failed to show a difference between the small bowel and the colon regarding the effect of local preimmunization with ovalbumin on the subsequent systemic immune response to this antigen, despite the functional and phenotypical differences recently described.

=> s antigen presentation
L23 ANTIGEN PRESENTATION

=> s l23 and dendritic cell
L24 L23 AND DENDRITIC CELL

=> s l24 and cytotoxic response

L25 35 L24 AND CYTOTOXIC RESPONSE

=> s l25 and lymph node
L26 6 L25 AND LYMPH NODE

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L27 4 DUP REMOVE L26 (2 DUPLICATES REMOVED)

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L27 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
2001:712021 Document No. 136:4679 Plasmid DNA encoding CCR7 ligands compen[illegible] for dysfunctional CD8+ T cell responses by effects on **dendri**[illegible]**cells.** Eo, Seong Kug; Kumaraguru, Udayas[illegible]; Rouse, Barry T. (Laboratory of Viral Immunology, Department of Mic[illegible]ology, University of Tennessee, Knoxville, TN, 37996, USA). Journal [illegible] Immunology, 167(7), 3592-3599 (English) 2001. CODEN: JOIMA3. ISSN: 0[illegible]2-1767. Publisher: American Association of Immunologists.
AB Lymphotoxin α-deficient (LTα-/-) mice, which lack **lymph** n[illegible]**es** and possess a disorganized spleen, develop dysfunctional CD8+ T cells upon HSV infection and readily succumb to herpes [illegible]ephalitis. Such mice do develop apparently normal peptid[illegible]cific CD8+ T cell responses, as measured by MHC class 1 tetram[illegible]taining, but the majority of cells fail to become cytotoxic or expres[illegible]tide-induced IFN-γ production In the present study, the authors [illegible]onstrate that functional defects of CD8+ T cells in LTα-/- m[illegible]e can be largely rectified by the administration of plasmid [illegible]A encoding CCR7 ligands before HSV infection. Treated mutant mice de[illegible]eloped increased peptide-specific **cytotoxic respon[illegible]s**, enhanced nos. of CD8+ T cells capable of producing IFN-γ, [illegible] well as improved resistance to HSV challenge. The corrective effect of chemokine treatment appeared to result from improved **dendr**[illegible]ell-mediated Ag presentation. Thus, a major conse[illegible] of the treatment was an increase in splenic **dendritic cell** [illegible] in CCR7 ligand-treated LTα-/- mice with such splen[illegible]populations showing improved APC activity in vitro. Our resul[illegible]ment that functional defects of CD8+ T cells can be corrected, and indi[illegible]ng value of plasmid vector encoding appropriate chemokines to achi[illegible]ch immunotherapy.

L27 ANSWER [illegible] 4 CAPLUS COPYRIGHT 2004 ACS on STN
2000:71768[illegible] cument No. 134:264700 **Dendritic cell** activ[illegible] by danger and antigen-specific T-cell signaling. McLellan, A. D.; B[illegible], E.-B.; Kampgen, E. (Department of Dermatology, University of Wuerz[illegible]Wuerzburg, 97080, Germany). Experimental Dermatology, 9(5), 313-3[illegible]glish) 2000. CODEN: EXDEEY. ISSN: 0906-6705. Publisher: Munks[illegible]nternational Publishers Ltd..
AB A rev[illegible] 99 refs. Recent transplantation, animal and in vitro studi[illegible]t a dependence of some immune reactions on tissue damage. Altho[illegible] factors involved in enhancing immune responses through tissu[illegible] have yet to be identified, recent data suggests that one of the t[illegible]f these cellular stress factors is the bone marrow derived **dendr**[illegible] (DC). DC are potent initiators of prima[illegible]mmune responses and hold the key to immune reactions through their [illegible]ty to sense changes in their local environment and respond appro[illegible]y to induce T-cell immunity, or possibly tolerance. In the **lymph**[illegible]DC are also influenced by antigen-specific signa[illegible]from T cells, which may extend and amplify DC antigen presenting capab[illegible]ie , especially for the stimulation of **cytotoxic respo**[illegible]. It now appears that both tissue damage and antig[illegible]pecific T-cell derived signals act together on the DC to promote the a[illegible]te immune reaction to antigen. Thus DC antigen presenting behav[illegible]ot only dependent on the context of antigen encounter in the perip[illegible]ry, but also on the availability of antigen-specific T cells and

their T-cell receptor specificities.

L27 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
2000:829825 Document No. 134:145994 **Dendritic cell** elimination as an assay of cytotoxic T lymphocyte activity in vivo. Ritchie, D. S.; Hermans, I. F.; Lumsden, J. M.; Scanga, C. B.; Roberts, J. M.; Yang, J.; Kemp, R. A.; Ronchese, F. (Malaghan Institute of Medical Research, Wellington School of Medicine, Wellington, N. Z.). Journal of Immunological Methods, 246(1-2), 109-117 (English) 2000. CODEN: JIMMBG. ISSN: 0022-1759. Publisher: Elsevier Science B.V..

AB We show in this paper that the survival of antigen-loaded **dendritic cells** in vivo may be used as a sensitive readout of CTL activity. We have previously shown that **dendritic cells** labeled with the fluorescent dye CFSE and injected subcutaneously into mice migrate spontaneously to the draining **lymph** nodes where they persist for several days. In the presence of effector CTL responses, **dendritic cells** loaded with specific antigen rapidly disappear from the draining **lymph node**. In this paper we extend the above observations and set up a simple and sensitive method to reveal CTL activity in individual mice in vivo. **Dendritic cells** were labeled with two different fluorochromes, loaded with antigen or left untreated, and mixed together before injection into mice. We show that only **dendritic cells** loaded with specific antigen were eliminated from the draining **lymph node**, while **dendritic cells** not loaded with antigen remained unaffected. Cytotoxic **responses** generated by immunization with peptide-loaded **dendritic cells**, or by infection with influenza virus, could be revealed using this method. Comparison of the differential survival of **dendritic cells** populations mixed together also allowed us to accurately evaluate the disappearance of **dendritic cells**, irresp. of variability in the injection site and other parameters. Given the ability of **dendritic cells** to efficiently take up and present exogenous antigens, nucleic acids and apoptotic bodies, this method may also allow the evaluation of cytotoxic activity against antigens that are not characterized in terms of peptide epitopes.

L27 ANSWER 4 OF 4 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 1
1999321139 [Strategies developed by HIV for escaping immune response]. STRATEGIES DEVELOPPEES PAR LE VIH POUR ECHAPPER AU SYSTEME IMMUNITAIRE DU VIH. Benaroch P.; Le Gall S.; Benaroch, Inserm U. 520, Institut Curie, Batiment Lhomond, 26 rue d'Ulm, 75248 Paris Cedex 05, France. Medecine/Sciences 15/8-9 (950-959).
Refs: 39.
ISSN: 0767-0974. CODEN: MSMSE4. Pub. Country: France. Language: French.
Summary Language: French; English.

AB HIV infection relies amazingly on **dendritic cells** (DC) for both, its replication and its ability to escape the immune system. DC are specialized in antigen **presentation** and possess the unique ability to stimulate naive T cells. In periphery, DC are spread in the mucosae where they represent the first cells that HIV can infect. They efficiently contribute in its spreading by migrating to **lymph** nodes, major site of infection. Infected DC can fuse to activated T cells to form syncitia that become fantastic factories of viral production. During the asymptomatic phase, follicular DC of **lymph** nodes trap HIV particles at their cell surface, representing the major reservoir of HIV. Thus, CD4+ T cells become infected by circulating through the dendritic network. HIV infection may impede DC capacity to present viral antigens and induce a decrease in DC numbers. Importantly, disappearance of DC is linked to the establishment of AIDS. Therefore, DC are key players at the different steps of HIV infection. HIV particles incorporate several human proteins, including MHC class II molecules, when budding from infected

cells. The role of these molecules is discussed in the light of recent results suggesting that they could be involved in the efficiency of virus entry as well as in neutralizing important components of the antiviral cellular response. **Antigen presentation** by MHC class II molecules might also be affected by the HIV infection. HIV has developed a strategy to down regulate surface MHC class I molecules, which allows infected cells to escape the **cytotoxic response**. This down modulation is mediated by the Nef protein, the expression of which modifies the intracellular trafficking of MHC class I molecules. Recent results suggest that Nef may connect them to the cellular machinery involved in transport to endocytic compartments from the plasma membrane as well as from the Golgi apparatus. Through its very high genomic variability, HIV creates numerous substitutions amongst the sequences encoding epitopes presented by MHC class I molecules and recognized by cytotoxic T cells. This may result in loss of presentation by MHC class I molecules, or in loss of T cell reactivity.

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L28 1253[illegible]4 METHOD

=> s l28 and inducing CTL response
L29 13 L[illegible] AND INDUCING CTL RESPONSE

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L30 6 DUP REMOVE L29 (7 DUPLICATES REMOVED)

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L30 ANSWER 1 OF 6 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
2003:130796 Document No.: PREV200300130796. Dendritic cell (DC) based therapy for cervical cancer: Use of DC pulsed with tumour lysate and matured with a novel synthetic clinically non-toxic double stranded RNA analogue poly (I):poly (C12U) (Ampligen(R)). Adams, M. [Reprint Author]; Navabi, H.; Jasani, B.; Man, S.; Fiander, A.; Evans, A. S.; Donninger, C.; Mason, M.. Velindre NHS Trust, Velindre Hospital, Whitchurch, Cardiff, CF 14 2TL, UK. mail[illegible].adam[illegible]@velindre-tr.wales.nhs.uk. Vaccine, (30 January 2003) Vol. 21, No. 7-8, pp. 787-790. print.
ISSN: 0264-410X (ISSN print). Language: English.
AB Human papilloma virus (HPV) found in 99.7% of cervical cancers represents an attractive immunotherapeutic target for novel adjuvant dendritic cell (DC) immunotherapy. DC primed with HPV antigens have been shown to be capable of inducing CTL **responses** powerful enough to eradicate established murine tumours expressing HPV16 antigen. The use of tumour lysate has been found to be an effective means of priming DC with tumour associated antigens in animal models and in clinical trials leading to significant anti-tumour responses. Autologous DC pulsed with sonicated HPV expressing tumour lysate have been shown to be capable of inducing HPV specific classes I and II T-cell immunity in a pilot clinical study. Synthetic double stranded polyribonucleotides are effective in vitro activation/maturation agents capable of inducing a stable mature DC phenotype producing high levels of IL12. However, the prototype polymer poly (I):poly (G) has proved to be clinically toxic. Preliminary in vitro data have demonstrated that a novel clinically non-toxic analogue polymer poly (I):poly (C12U) (Ampligen(R)) can effectively enhance in vitro maturation of human monocyte derived DC with sustained productive IL12 production. Human monocyte derived DC primed with tumour lysate and matured with synthetic dsRNA may therefore offer an effective way of optimising Th1 specific anti-cancer T-cell responses in cancer patients. This strategy is currently being tested in a clinical trial of patients with cervical cancer.

L30 ANSWER 2 OF 6 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
2001:331113 Document No.: PREV200100331113. Immunization with a

tumor-associated CTL epitope plus a tumor-related or unrelated Th1 helper pept[illegible] elicits protective CTL immunity. Casares, Noelia; Lasarte, Juan Jose [illegible]t author]; Lopez-Diaz de Cerio, Ascension; Sarobe, Pablo; Ruiz, [illegible] Melero, Ignacio; Prieto, Jesus; Borras-Cuesta, Francisco [Repr[illegible]hor]. Departamento de Medicina Interna, Facultad de Medicina, Univ[illegible]de de Navarra, Irunlarrea 1, E-31008, Pamplona, Spain. jjlas[illegible]e@[illegible].es; fborras@unav.es. European Journal of Immunology, (June, 2001) [illegible]ol. 31, No. 6, pp. 1780-1789. print.
CODEN: [illegible]JIMAF. ISSN: 0014-2980. Language: English.

AB Immun[illegible]tion with cytotoxic T cell epitope SPSYVYHQF (AH1), derived from MuLV [illegible] envelope protein expressed by CT26 tumor cells, does not protect BALB/[illegible] against challenge with CT26 tumor cells. By contrast, imm[illegible]n with AH1 plus T helper peptides OVA(323-337) or SWM(106-118) elic[illegible]1 and Th0 profiles, protected 83% and 33% of mice, resp[illegible]. Interestingly, immunization with AH1 plus both helper pep[illegible]rted the efficacy to 33%. We identified the endogenous T hel[illegible]p(320-333) from gp70 which elicits a Th1 profile and is nat[illegible]y[illegible]ed. As for OVA(323-337), immunization with p(320-333) alone [illegible]protect against tumor challenge. However, p(320-333) plus AH1 p[illegible]ed 8[illegible]% of mice at day 10 after vaccination. Only 20% of mice vac[illegible]ed with AH1+OVA(323-337) or AH1+p(320-333) were protected when cha[illegible]90 days after immunization. Treatment with OVA(323-337) or wit[illegible]ground established tumors delayed tumor growth. Our re[illegible] tumor-related as well as tumor-unrelated but strong Th1 pe[illegible]useful for **inducing CTL** **re**[illegible]r immunotherapy.

L30 AN[illegible]OSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
2001:29[illegible] No.: PREV200100291318. Protein sigma1-mediated DNA im[illegible]inst HIV. Maj, Jerzy G. [Reprint author]; Hone, D. M.; Shal[illegible]equal, D. W. [Reprint author]. Veterinary Molecular Biolo[illegible]State University, Bozeman, MT, 59717-3610, USA. FASEB Journ[illegible], 2001) Vol. 15, No. 4, pp. A364. print.
Me[illegible]nual Meeting of the Federation of American Societies for Ex[illegible]ogy on Experimental Biology 2001. Orlando, Florida, USA. Ma[illegible], 2001.
CO[illegible]SN: 0892-6638. Language: English.

AB To [illegible]l immunity, we have adapted M cell-directed DNA va[illegible]a[illegible] the M cell ligand, protein sigma1 from reovirus. We ef[illegible]tiv[illegible]fected protein sigma1 receptor-positive cells with the co[illegible]ain sigma1 and poly-L-lysine (PL) combined with plasmid DN[illegible]. I[illegible]c[illegible]eriments, groups of BALB/c mice were intranasally (i.n.) im[illegible]d[illegible]formulated, PL-DNA, or naked DNA encoding HIV (Bal) gp160 at on[illegible]n[illegible]vals for a total of three doses. Four weeks after the la[illegible], lymphocytes from local and distal tissues were examined fo[illegible]by a standard 51Cr release assay. Ex vivo lung, spleen an[illegible]a formulated gp160-immunized mice showed 69.2%, 16.0% an[illegible]p[illegible]cytotoxic lysis of envelope-expressing targets, while an[illegible]ti[illegible]ated splenic, LRLN, cervical LN, and parotid LN cells pr[illegible]e[illegible].4[illegible]%, 29.2% and 30.2% specific lysis, respectively. Fr[illegible]an[illegible]ed lymphocytes isolated from PL-DNA or naked DNA im[illegible]iz[illegible]failed to exert cytolysis. Compared to standard at[illegible]uated [illegible]ctors, we conclude that our mucosal formulation is a safe, effe[illegible]iv[illegible]nd tissue-specific **method** for **inducing** **CTL** [illegible]por[illegible]ainst HIV.

L30 ANSW[illegible]4 C[illegible]MEDLINE on STN
200214586[illegible] ID: 11877044. Preliminary study on CTL enhancement indu[illegible]by I[illegible]modified HL-60 cells. Li C; Fu J. (Shenzhen Chil[illegible]Ho[illegible]l, Shenzhen 518026, China.) Zhonghua xue ye xue za zhi = Zh[illegible]xue[illegible]zazhi, (2001 Jan) 22 (1) 17-9. Journal code: 8212398. ISSN: [illegible]272, Pub. country: China. Language: Chinese.

AB OBJEC[illegible]. To e[illegible]re the mechanism of enhancing killing activity of tumor cell-s[illegible]eci[illegible]c[illegible]otoxic T lymphocyte (CTL) by IL-4 gene modified tumor cells (IL-[illegible]. METHODS: IL-4 gene was introduced into HL-60

cells thro[illegible]h r[illegible]troviral vector PL-IL-4-SN. Wild and IL-4 mTC were used to i[illegible]duce [illegible] responses, and cell surface molecules were assayed by flow cyto[illegible]ry. RESULTS: The killing activity of tumor cell-specific CTL in IL-4 [illegible] g[illegible] was increased from 11.8% to 77.2%, about sevenfold higher than [illegible] by wild HL-60 cells (P < 0.01). High level expression of MH[illegible]lar[illegible]f antigens as well as B7-1 and ICAM-1 molecules was observed in IL-[illegible] mT[illegible]. The expression of MHC class I antigen was not affected by IL-4 g[illegible]ne [illegible]odification. The expression of cell surface molecules induced by IL-4 mT[illegible] was completely abrogated by anti-IL-4 McAb. A significant increase o[illegible] IL-[illegible] secretions was detected during IL-4 mTC **inducing CTL** r[illegible]. IL-2 secretion and CTL response were inhi[illegible] [illegible]-IL-4 or anti-surface molecule McAbs. CONCLUSION: IL-4 gene [illegible]ight enhance the tumor cell-specific CTL killing acti[illegible]ing cell surface molecules expression and IL-2 secre[illegible].

L30 ANSWE[illegible] MEDLINE on STN DUPLICATE 1
1998430684[illegible]: 9759884. Controlled lipidation and encapsulation of pepti[illegible]s a[illegible] approach to mucosal immunizations. Mora A L; Tam J P. (Depa[illegible]ner[illegible]r Biology and Immunology, Vanderbilt University, Nash[illegible]-2363, USA.) Journal of immunology (Baltimore, Md. : 1950) [illegible]) 161 (7) 3616-23. Journal code: 2985117R. ISSN: 002[illegible]ountry: United States. Language: English.
AB To g[illegible]l strategy for mucosal immunization, we have developed an a[illegible]ipating a multiple Ag peptide (MAP) containing part of the V3 [illegible]r HIV-1 gp120IIIB. In this work, we compare two delivery system[illegible] MAP in PBS and encapsulation in poly(DL-lactide-co-glycol[illegible]e) [illegible]particles. Subcutaneous immunization, followed by intrac[illegible]ministration of MAP peptide entrapped or not entrapped in micro[illegible]ased mucosal and systemic immune responses at local and dista[illegible]ing mucosal IgA in saliva, vaginal secretions and fec[illegible]blood. However, lipidated Ag delivered in mi[illegible]t higher levels of mucosal Abs, particularly of int[illegible]sti[illegible]nerated CTL responses. In contrast, lipidated MAP deliver[illegible]te microparticles was less effective in **inducir**[illegible]. These results demons[illegible]ility of using a lipidated multimeric peptide for mucosa[illegible] to stimulate both systemic and mucosal immune system[illegible]e genital tract, irrespective of the route or **me**th[illegible]and without requiring the use of a carrier or an ex[illegible]t.

L30 AN[illegible]LINE on STN DUPLICATE 2
9624596[illegible]8376. Induction of single and dual cytotoxic T-[illegible]mpl[illegible]s to viral proteins in mice using recombinant hybrid Ty-[illegible]iru[illegible]. Layton G T; Harris S J; Myhan J; West D; Gotch F; Hi[illegible]l-Pe[illegible]k[illegible] S; Meyers N; Woodrow S; French T J; Adams S E; Ki[illegible]gsm[illegible] Biotech Pharmaceuticals Ltd, Oxford, UK.) Im[illegible]no[illegible] [illegible]b 87 (2) 171-8. Journal code: 0374672. ISSN: 0019-2[illegible]ountry: ENGLAND: United Kingdom. Language: English.
AB Th[illegible]in[illegible]xic T-lymphocyte (CTL) responses to viral proteins is [illegible]hou[illegible]ssential component of protective immunity against vi[illegible]l i[illegible]ods for generating such responses in a re[illegible]d[illegible]uld be of great value in vaccine development. We de[illegible]the recombinant antigen-presentation system based on th[illegible]e[illegible] (Ty) particle-forming p1 protein is a potent means of **ir**[illegible]i[illegible] to a variety of viral CT[illegible]ep[illegible]g influenza virus nucleoprotein (two epitopes), Se[illegible]ular stomatitis virus nucleoproteins, and the V3 lo[illegible]ficiency virus type-1 (HIV-1) gp120. CTL were pr[illegible]us-like particles (VLP) carrying the minimal epi[illegible]pe[illegible]n 9,000 MW of protein. Ty-VLP carrying two different epi[illegible]pe[illegible] Ty-VLP) were capable of priming CTL responses in two di[illegible]t[illegible]f mice or against two epitopes in the same ir[illegible]he[illegible]e, co-administration of a mixture of two different

Ty-VLP [illegible] single epitopes could induce responses to both epitopes in th[illegible] individual Ty-VLP appear to represent a reproducible and fl[illegible]m fo[illegible] **nducing CTL responses** in [illegible]arra[illegible] further evaluation in primates.

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